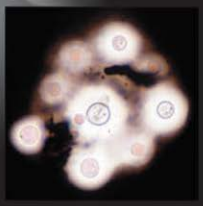
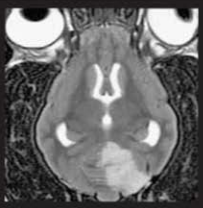
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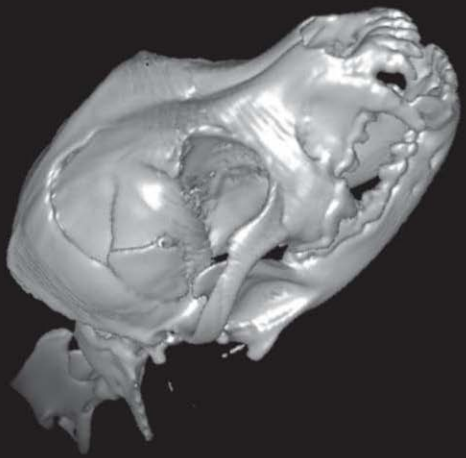
Simon Platt • Laurent Garosi











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Small Animal Neurological Emergencies

SIMON R PLATT BVM&S, DipACVIM(NEUROLOGY), DipECVN, MRCVS

Professor Neurology Service
Department of Small Animal Medicine and Surgery
College of Veterinary Medicine
University of Georgia
Athens, Georgia, USA

LAURENT S GAROSI DVM, DipECVN, MRCVS

Director and Head of Neurology/Neurosurgery Service
Davies Veterinary Specialists
Higham Gobion
Hertfordshire, England, UK

MANSON PUBLISHING/THE VETERINARY PRESS

For my girls, Jade, Danielle and Georgina
Simon Platt

To my son, George
Laurent Garosi

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CONTRIBUTORS

Kerry Smith Bailey
DVM, DipACVIM(Neurology)
Oradell Animal Hospital
Paramus, New Jersey, USA

Sebastien Behr
DVM, DipECVN, MRCVS
Willows Veterinary Centre and Referral Service
Shirley,
Solihull, West Midlands, UK

Benjamin M Brainard
VMD, DipACVA, DipACVECC
Department of Small Animal Medicine and Surgery
College of Veterinary Medicine
University of Georgia
Athens, Georgia, USA

Kate E Chandler
BVetMed, PhD, DipECVN, FHEA, MRCVS
Park Road
Northaw,
Hertfordshire, UK

Louise Clark
BVMS, DipECVAA, CertVA, MRCVS
Davies Veterinary Specialists
Higham Gobion, Hertfordshire, UK

Joan R Coates
DVM, MS, DipACVIM(Neurology)
Department of Veterinary Medicine and Surgery
College of Veterinary Medicine
University of Missouri
Columbia, Missouri, USA

Ronaldo C da Costa
DVM, MSc, PhD, DipACVIM(Neurology)
Department of Veterinary Clinical Sciences
College of Veterinary Medicine
The Ohio State University
Columbus, Ohio, USA

Peter J Dickinson
BVSc, PhD, DipACVIM(Neurology)
Department of Surgical and Radiological Sciences
School of Veterinary Medicine
University of California-Davis
Davis, California, USA

Courtenay Freeman
DVM
Department of Small Animal Medicine and Surgery
College of Veterinary Medicine
University of Georgia
Athens, Georgia, USA

Laurent S Garosi
DVM, DipECVN, MRCVS
Davies Veterinary Specialists
Higham Gobion, Hertfordshire, UK

Toby J Gemmill
BVSc, MVM, DSAS(Orth), DipECVS, MRCVS
Willows Veterinary Centre and Referral Service
Shirley,
Solihull, West Midlands, UK

Robert A N Goggs
BVSc, DipACVECC, MRCVS
Faculty of Medical and Veterinary Sciences
University of Bristol
Bristol, UK

Rebecca J Green
BSc (Hons), ABW, RVN, CertCH
Davies Veterinary Specialists
Higham Gobion, Hertfordshire, UK

Allison C Haley
BSc, DVM, MRCVS
Faculty of Veterinary Medicine
University of Glasgow
Bearsden Road
Glasgow, UK

Marc Kent
DVM, DipACVIM(Internal Medicine and Neurology)
Department of Small Animal Medicine and Surgery
College of Veterinary Medicine
University of Georgia
Athens, Georgia, USA

Jonathan M Levine
DVM, DipACVIM(Neurology)
Department of Small Animal Clinical Sciences
College of Veterinary Medicine
Texas A&M University
College Station, Texas, USA

Lara A Matiasek
DrMedVet, DipECVN, MRCVS
Clinic of Small Animal Medicine
at the Centre for Clinical
Veterinary Medicine,
Veterinary Faculty, LMU Munich
Munich, Germany

J Fraser McConnell
BVM&S, DipECVDI, DVR,
CertSAM, MRCVS
Small Animal Teaching Hospital
Faculty of Veterinary Science
University of Liverpool
Leahurst
Neston, Wirral, UK

John J McDonnell
DVM, MS, DipACVIM(Neurology)
Veterinary Neurology of the
Chesapeake
Annapolis
Maryland, USA

W Malcolm McKee
BVMS, MVS, DSAO, MACVSc,
MRCVS
Willows Veterinary Centre and
Referral Service
Shirley,
Solihull, West Midlands, UK

Gabrielle C Musk
BSc, BVMS, CertVA, DipECVAA
Veterinary Clinical Sciences
Division of Veterinary and
Biomedical Sciences
Murdoch University
Perth, Western Australia, Australia

Arianna Negrin
DVM, PhD
Faculty of Veterinary Medicine
University of Padova
Legnaro, Padova, Italy

Peter P Nghiem
DVM
Center for Genetic Medicine
Research
Children's National Medical Center
Washington DC, USA

Natasha J Olby
MA, VetMB, PhD,
DipACVIM(Neurology), MRCVS
Department of Clinical Sciences
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina, USA

Theresa Pancotto
DVM, MS
Virginia-Maryland Regional
College of Veterinary Medicine
Virginia Tech
Blacksburg, Virginia, USA

Jacques Penderis
BVSc, MVM, PhD, CertVR,
DipECVN, MRCVS
Faculty of Veterinary Medicine
University of Glasgow
Bearsden Road
Glasgow, UK

Jennifer Pittman
DVM, DipACVECC
Georgia Veterinary Specialists
Atlanta, Georgia, USA

Simon R Platt
BVM&S, DipACVIM(Neurology),
DipECVN, MRCVS
Department of Small Animal
Medicine and Surgery
College of Veterinary Medicine
University of Georgia
Athens, Georgia, USA

Anthea L Raisis
BVSc, PhD, DVA, MACVSc,
MRCVS, MVetClinSt
Veterinary Clinical Sciences
Division of Veterinary and
Biomedical Sciences
Murdoch University
Perth, Western Australia, Australia

Luisa de Risio
DVM, PhD, DipECVN, MRCVS
Centre for Small Animal Studies
Animal Health Trust
Lanwades Park
Newmarket, Suffolk, UK

John H Rossmeisl Jr.
DVM, MS, DipACVCIM
(Internal Medicine and Neurology)
Virginia-Maryland Regional
College of Veterinary Medicine
Virginia Tech
Blacksburg, Virginia, USA

Scott Schatzberg
DVM, PhD,
DiplACVIM(Neurology)
Veterinary Emergency & Specialty
Centers LLC
2001 Vivigen Way
Santa Fe, NM 87505, USA

Alberta de Stefani
DVM, PhD, DipECVN, MRCVS
Centre for Small Animal Studies
Animal Health Trust
Lanwades Park
Newmarket, Suffolk, UK

Katrin Swindells
BVSc, MACVSc, DipACVECC
Veterinary Clinical Sciences
School of Veterinary and
Biomedical Science
Murdoch University
Perth, Western Australia, Australia

Amy J Wood
DVM
Department of Small Animal
Clinical Sciences
Veterinary Teaching Hospital
University of Tennessee
Knoxville, Tennessee, USA

PREFACE

THE field of clinical veterinary neurology has expanded dramatically over the last couple of decades due in part to the increased availability of advanced imaging facilities, improved dispersion of knowledge through electronic media and greater consumer demand for therapy in the face of an unknown prognosis. A large part of this field is emergency based and many neurology patients will require critical care. Rapid and practical decisions often need to be made based on uncertain diagnoses and prognoses and frequently accompanied by restricted finances. Couple this with a justifiable fear of clinical neurology and we find ourselves faced with an extremely challenging genre of cases.

Such daily challenges prompted our interest in the project that has become this book. Our aim was to develop a textbook that addressed small animal neurological emergencies on multiple levels. The main focus was always the need to be able to address cases quickly based on their presenting syndrome, whether this be seizures, head tilt or paralysis. The chapters in Part 2 of this book have therefore been the fulcrum from which everything else developed. In addition to the practical aspect, it is essential to have an in-depth section addressing the most common specific emergencies on a pathophysiological, therapeutic and prognostic basis. This is dealt with in Part 3 and hopefully will be beneficial to practitioners, students, residents and specialists alike. More detailed diagnostic and emergency supportive therapies have been addressed in Parts 1 and 4, respectively, and should be informative to those with imaging, critical care, anaesthesia, pathology and neurology interests. With this multi-level goal in mind, we have put together an outstanding array of experts in these fields, who have provided not only up-to-date information, but also invaluable opinion on how to deal with the vast range of neurological emergencies. What we hope we have also achieved with this group of authors is a more global approach than is typical for such a focused text. Specialists from Australia, Europe and the USA have helped achieve this goal and we are deeply indebted to all of them for their contributions.

We are grateful to the students, residents and practitioners whom we have been fortunate enough to work with and who have helped us understand what is needed in a book such as this. We would also like to thank our mentors and colleagues, too numerous to mention, who have inspired us to be who and what we are. However, Simon wishes to personally thank Dr Cheryl Chrisman for her guidance, sincerity, knowledge, passion for neurology and friendship; and Laurent would like to thank Dr Laurent Cauzinille, Dr Alexander de Lahunta and Professor Jacques Penderis. Final thanks should go to Jill Northcott and all of those at Manson Publishing who have believed in this project and supported us over the time it has taken to be completed.

We hope that you enjoy this text and that in some way it helps you feel more comfortable with the next neurological emergency.

Simon Platt and Laurent Garosi

ABBREVIATIONS

AA	atlantoaxial
AAROM	active assisted range of motion
ACD-A	acid citrate dextrose-A
ACE	angiotensin-converting enzyme
acetyl CoA	acetyl coenzyme A
ACh	acetylcholine
AChE	acetylcholinesterase
AChR	acetylcholine receptor
ACT	activated clotting time
ACTH	adrenocorticotropic hormone
ADC	apparent diffusion coefficient
ADH	antidiuretic hormone
ADP	adenosine diphosphate
AED	antiepileptic drug
AGID	agar gel immunodiffusion
AH	abductor halluci
ALI	acute lung injury
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AMG	acquired myasthenia gravis
AMPA	alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid
ANNPE	acute non-compressive nucleus pulposus extrusion
ANP	atrial natriuretic peptide
APPs	acute phase proteins
aPTT	activated partial thromboplastin time
ARAS	ascending reticular activating system
ARDS	acute respiratory distress syndrome
AROM	assisted range of motion
AST	aspartate aminotransferase
AT	antithrombin
ATP	adenosine triphosphate
AV	atrioventricular
BAER	brainstem auditory evoked response
BMBTs	buccal mucosal bleeding times
BP	blood pressure
bpm	beats per minute
BUN	blood urea nitrogen
CA	cytosine arabinoside
cAMP	cyclic adenosine monophosphate
CaO_2	arterial oxygen content
CAT	choline acetyltransferase
CBC	complete blood count
CBF	cerebral blood flow
CDI	central diabetes insipidus
CDV	canine distemper virus
CHEM	serum chemistry panel
CK	creatine kinase
CMAP	compound muscle action potential
CMC	cerebellomedullary cistern
CMG	congenital myasthenia gravis
CMOP	craniomandibular osteopathy
CMR	cerebral metabolic rate
CN	cranial nerve
CNS	central nervous system
CO	cardiac output
CO_2	carbon dioxide
CoA	coenzyme A
COP	colloid osmotic pressure
CPAP	continuous positive airway pressure
CPCR	cardio–pulmonary–cerebral resuscitation
CPDA-1	citrate phosphate dextrose adenine-1
CPP	cerebral perfusion pressure
CRI	constant rate infusion
CRP	C-reactive protein
CRT	capillary refill time
CS	chondroitin sulphate
CSF	cerebrospinal fluid
CSM	cervical spondylomyelopathy
CT	computed tomography
CVA	cerebrovascular accident
CVP	central venous pressure
CVR	cerebral vascular resistance
D5W	5% dextrose in water
DDS	dialysis disequilibrium syndrome
DEA	dog erythrocyte antigen
DEET	diethyltoluamide
DI	diabetes insipidus

DIC	disseminated intravascular coagulation
DINAMAP	device for indirect non-invasive, automated, mean arterial pressure
DISH	disseminated idiopathic skeletal hyperostosis
DNA	deoxyribonucleic acid
DO_2	oxygen delivery
DTPA	diethylenetriamine penta-acetic acid
DV	dorsoventral
DWI	diffusion-weighted imaging
ECF	extracellular fluid
ECG	electrocardiogram
EDB	extensor digitorum brevis
EDTA	ethylenediamine tetra-acetic acid
EEG	electroencephalogram
ELISA	enzyme-linked immunosorbent assay
EME	eosinophilic meningoencephalomyelitis
EMG	electromyogram
EMLA	eutectic mixture of local anaesthetics
EMS	electrical muscle stimulation
EPP	end plate potential
ERG	electroretinogram
ETT	endotracheal tube
$FADH_2$	reduced form of flavin adenine dinucleotide
Fat Sat	fat saturation (image)
FCE	fibrocartilaginous embolism
FCEM	fibrocartilaginous embolic myelopathy
FDP	fibrin (fibrinogen) degradation product
$F'ECO_2$	fractional concentration of carbon dioxide in mixed expired air
FeLV	feline leukaemia virus
FFP	fresh frozen plasma
FHS	feline hyperaesthesia syndrome
FiO_2	fractional concentration of oxygen in inspired air
FIP	feline infectious peritonitis
FLAIR	fluid attenuated inversion recovery (image)
FSE	fast spin echo (image)
fT4	free thyroxine
GA	general anaesthesia
GABA	gamma-aminobutyric acid
GAG	glycosaminoglycan
GCMPS	Glasgow Composite Measure Pain Scale
GCS	Glasgow coma scale
GFAP	glial fibrillary acid protein
GFR	glomerular filtration rate
GI	gastrointestinal
GME	granulomatous meningoencephalitis
GP	general proprioceptive (ataxia/system)
GRE	gradient-echo (images)
GTP	guanosine triphosphate
5-HT	5-hydroxytryptamine
Hb	haemoglobin
HCO_3^-	bicarbonate
HE	hepatic encephalopathy
HME	heat and moisture exchange
HR	heart rate
HRPO	horse-radish peroxidase
HTIG	human tetanus immunoglobulin
IABP	invasive arterial blood pressure
iCa^{2+}	ionized calcium concentration
ICF	intracellular fluid
ICP	intracranial pressure
ICU	intensive care unit
ID	intradermal
IFA	immunofluorescent antibody
Ig	immunoglobulin
IGF-1	insulin-like growth factor-1
IHC	immunohistochemistry
IL-1	interleukin-1
IM	intramuscular
IN	intranasal
iNOS	ionized nitric oxide synthetase
IPPV	intermittent positive pressure ventilation
ITN	idiopathic trigeminal neuropathy/neuritis
IV	intravenous
IVDD	intervertebral disc disease
KBr	potassium bromide
kPa	kilopascal
KS	keratan sulphate
L	lactate
L:P	lactate:pyruvate ratio
L2-HGA	L2-hydroxyglutaric aciduria
LD_{50}	median lethal dose
LGN	lateral geniculate nucleus/i
LMN	lower motor neuron
LS	lumbosacral
MABP	mean arterial blood pressure
MAC	minimum alveolar concentration
MAP	mean arterial pressure
ME	meningoencephalitis
MEM	meningoencephalomyelitis
MG	myasthenia gravis
MGCS	Modified Glasgow Coma Scale

MIR	main immunogenic region
MLAER	middle latency auditory evoked response
MMC	mitochondrial membrane megachannel
MMM	masticatory muscle myositis
MNCV	motor nerve conduction velocity
MOF	multiple organ failure
MPSS	methylprednisolone sodium succinate
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MUA	meningoencephalitis of unknown aetiology
MUP	motor unit potential
MW	molecular weight
$NaHCO_3$	sodium bicarbonate
NADH	nicotinamide adenine dinucleotide
NASCIS	National Acute Spinal Cord Injury Study (trials)
NIBP	non-invasive arterial blood pressure
NLE	necrotizing leucoencephalitis
NM	neuromuscular
NMDA	N-methyl-D-aspartate
NME	necrotizing meningoencephalitis
NMES	neuromuscular electrical stimulation
NO	nitric oxide
N_2O	nitrous oxide
NSAID	nonsteroidal anti-inflammatory drug
NSE	neuron-specific enolase
OCD	osteochondrosis dissecans
OH	obstructive hydrocephalus
OP	organophosphate
OPIDN	organophosphate-induced delayed neuropathy
P	pyruvate
$PaCO_2$	arterial carbon dioxide partial pressure
$PACO_2$	alveolar carbon dioxide partial pressure
2-PAM	pralidoxime (2-pyridine aldoxime methyl chloride)
PaO_2	arterial oxygen partial pressure
PAO_2	alveolar oxygen partial pressure
PARP-	poly[ADP-ribose] polymerase-1
PARR	PCR for antigen receptor rearrangement
PBT	primary brain tumour
PCO_2	partial pressure of CO_2
PCP	phencyclidine
PCR	polymerase chain reaction
PCV	packed cell volume
PD	proton density (image)
PDH	pituitary-dependent hyperadrenocorticism
PDS	paroxysmal depolarizing shift
PEEP	positive end-expiratory pressure
PEG	polyethylene glycol
$P'ETCO_2$	end-tidal carbon dioxide partial pressure
PHPTH	primary hyperparathyroidism
PIP	peak inspiratory pressure
PLR	pupillary light reflex
PMMA	polymethyl methacrylate (cement)
PMN	polymorphonuclear (cells)
PNS	peripheral nervous system
PR	per rectum
PROM	passive range of motion
PSS	portosystemic shunt
PT	prothrombin time
PTH	parathyroid hormone
PTHrP	parathyroid hormone-related protein
PTN	pretectal nucleus
PTT	partial thromboplastin time
PU/PD	polyuria/polydipsia
PVE	plasma volume expansion
RAS	reticular activating system
RBC	red blood cell
REM	rapid eye movement
ROM	range of motion
ROS	reactive oxygen species
RR	respiratory rate
RTA	road traffic accident
SAE	sepsis-associated encephalopathy
SAP	systolic arterial blood pressure
SARDS	sudden acquired retinal degeneration syndrome
SBT	[1] secondary brain tumour
SBT	[2] systemic blood pressure
SC	subcutaneous
SE	status epilepticus
SF-EMG	single-fibre electromyography
SG	specific gravity
SIADH	syndrome of inappropriate antidiuretic hormone secretion
SIRS	systemic inflammatory response syndrome
SMFA	sodium monofluoroacetate
SNAR	soluble NSF attachment protein receptor
SPA	staphylococcal protein A
SpO_2	saturation of haemoglobin with oxygen
SRMA	steroid responsive meningitis–arteritis
SSEPs	somatosensory evoked potentials
STIR	short-tau inversion recovery (image)
SV	stroke volume
SVR	systemic vascular resistance

$T_{1/2}$	half-life
T1W	T1-weighted (image)
T2*GRE	T2* gradient-echo (image)
T2W	T2-weighted (image)
T3	triiodothyronine
T4	thyroxine
TCA	tricarboxylic acid
TCI	target controlled infusion
TENS	transcutaneous electrical nerve stimulation
TFPI	tissue factor pathway inhibitor
TIA	transient ischaemic attack
TIVA	total intravenous anaesthesia
TMJ	temporomandibular joint
TMS	trimethoprim–sulphonamide
TNCC	total nucleated cell count
TNF-α	tumour necrosis factor-alpha
TOD	target organ damage
TP	total protein
TPR	temperature, pulse, respiration
TS	total solids
TSH	thyroid-stimulating hormone
TSS	approximate time to steady state
tT4	total thyroxine
UA	urinalysis
UMN	upper motor neuron
UOP	urine output
URT	upper respiratory tract
USG	urine specific gravity
UTI	urinary tract infection
VC	vasoconstriction
VD	[1] vasodilatation
VD	[2] ventrodorsal
VEGF	vascular endothelial growth factor
VILI	ventilator-induced lung injury
VP	ventriculoperitoneal
V_T	tidal volume
WBC	white blood cell

PART 1

ADMISSION AND NEURODIAGNOSTIC TESTS

CHAPTER **1**	Examining the neurological emergency
CHAPTER **2**	Respiratory and cardiovascular support
CHAPTER **3**	Metabolic evaluation of critically ill neurological patients
CHAPTER **4**	Imaging of neurological emergencies
CHAPTER **5**	Cerebrospinal fluid analysis

EXAMINING THE NEUROLOGICAL EMERGENCY

Laurent Garosi

INTRODUCTION

Neurological emergencies require rapid and accurate decision making and treatment. Inappropriate management in the early stages of the disease can have catastrophic consequences for the animal. The aims of this chapter are to describe the step-by-step approach to the neurological emergency, including primary survey examination, rationale and principles of lesion localization within the nervous system, and how to establish a differential diagnosis list.

PRELIMINARY SURVEY EXAMINATION

It is all too tempting when presented with an emergency patient that has severe neurological signs to rush into evaluating its nervous system. However, initial physical assessment should focus on any imminent life-threatening abnormalities and evaluation of vital functions (see Chapter 2), all of which can influence not only the interpretation of the neurological examination, but also the prognosis for the patient. Preliminary survey examination assures identification and immediate treatment of conditions that are life threatening.

On arrival, every animal should be evaluated to determine whether it is stable, requires treatment of immediate life-threatening conditions and/or requires appropriate monitoring so that potential problems can be anticipated and prevented. Four major organ systems should be evaluated as part of the preliminary survey examination: respiratory, cardiovascular, urinary and neurological (*Table 1*). While the animal is being evaluated during the preliminary survey examination, the owners must be encouraged to give a clear and concise description of their concerns.

After the preliminary survey examination and stabilization of immediate life-threatening conditions, the secondary evaluation is performed. It is during this time that a detailed anamnesis is obtained from the owner and a comprehensive neurological examination performed. Other body systems should also be evaluated, with a complete physical examination to detect abnormalities that might affect the nervous system (e.g. animals presented for epileptic seizures and abnormal mentation that have liver disease), that mimic a primary neurological disorder (e.g. bilateral cruciate ligament rupture in an animal presented for a hindlimb gait abnormality) or that could influence the prognosis (e.g. bladder rupture in an animal with a traumatic spinal fracture).

Table 1 Initial assessment of the neurological emergency patient

Respiratory system	
Respiratory rate, effort and rhythm, patency of upper airway, auscultation of trachea and all areas of thorax	
Cardiovascular system	
Mucous membrane colour, capillary refill time, pulse rate, quality and rhythm, auscultation of the heart	
Renal system	
Ability to urinate and palpation of urinary bladder	
Neurological system	
Evaluation of mentation, ability to ambulate and pain perception	

ANAMNESIS

The onset, evolution and course of the illness are of paramount importance and may provide insight into specific differentials. Through careful questioning, the onset should be defined as peracute to acute (onset over minutes to hours), subacute (onset over days), chronic (onset over several days, weeks or months) or episodic (animal returns to normal in between episodes).

The evolution of the signs should be recognized as progressive, static, improving or waxing and waning. Factors that trigger or improve the signs and previous therapy and its effect on disease course are also important to identify. After determining the chief complaint, collecting the history should end with general information regarding any previous medical or surgical conditions, current medications, family history, vaccination status, diet, previous travel history, drug reactions and the animal's environment, including the potential for toxin exposure.

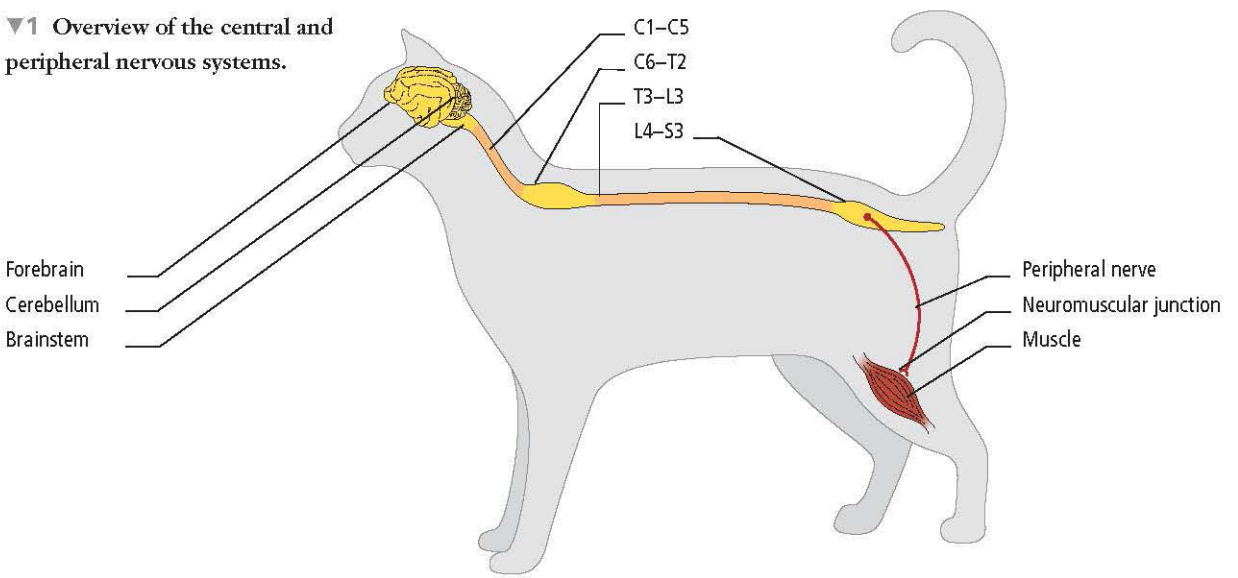
AIMS OF THE NEUROLOGICAL EXAMINATION

Before rushing into the specifics of the neurological examination, attention should be focused on what questions need to be answered:

- Do the clinical signs observed refer to a nervous system lesion?
- What is the location of this lesion within the nervous system?
- What are the main types of disease process that can explain the clinical signs?
- How severe is the disease?

The first two questions are answered by performing a general physical and neurological examination with a view to defining the neuroanatomical diagnosis (location and distribution of the lesion within the nervous system). By simple observation and testing a number of reflexes and responses (see Hands-off examination [p. 17] and Hands-on examination [p. 22]), the clinician should be able to determine if the animal is neurologically sound or not.

The neurological examination aims to test the integrity of the various components of the nervous system and, if present, detect any functional deficits. Normal findings are as important as the abnormal ones in localizing the lesion. Neurological abnormalities detected on examination should be noted and added to the list of abnormal findings collected from the history. Each of these abnormal findings should then be correlated to a specific region or to specific pathways within the peripheral and/or central nervous system (CNS). An attempt should then be made to explain all of the abnormal findings by a single lesion within one of the regions of the central and peripheral nervous systems, as illustrated in **1**: (i.e. focal forebrain, brainstem, cerebellum, C1–C5 spinal cord segments, C6–T2 spinal cord segments, T3–L3 spinal cord segments, L4–S3 spinal cord segments, peripheral nerve, neuromuscular junction, muscle). Lesions within these regions result in predictable and specific neurological signs. Note that in localizing a lesion, it is not necessary for all the clinical signs referable to one location or syndrome to be present. If a single lesion cannot explain all the listed abnormal findings, the lesion localization is considered as multifocal or diffuse.



▼1 Overview of the central and peripheral nervous systems.

The third question is answered by compiling information on the patient signalment and history of the problem with the neuroanatomical diagnosis in order to determine the differential diagnosis list. Disease severity helps to determine the prognosis of the differential diagnoses. Diagnostic tests are then carried out to investigate the differential diagnoses. The choice and interpretation of these tests must rely on a clear knowledge of the lesion localization within the nervous system and the expected disease processes.

RATIONALE AND PRINCIPLES OF LESION LOCALIZATION

The purpose of the neurological examination is to determine the neurologic abnormalities and, based on that, the location of the lesion or lesions responsible for causing these abnormalities. The location is the anatomical diagnosis. Narrowing down which part(s) of the nervous system may be affected can present a number of advantages:

- From a diagnostic point of view, the differential diagnosis is very dependent on the anatomical diagnosis.
- Aside from determining which part of the nervous system is affected, localizing the lesion also involves determining if the problem is focal, multifocal (i.e. affecting multiple parts of the nervous system) or diffuse (i.e. affecting globally and symmetrically one or more parts of the nervous system). Such information can then be used to further narrow down the differential list (see How to establish a differential diagnosis list, p. 33).
- A number of disease processes may only be diagnosed by exclusion of other causes mimicking a similar clinical history and presentation. This process of exclusion implies evaluating the correct part of the nervous system in order confidently to rule out these similar clinical diseases. Failure to localize the lesion, the interpretation of negative diagnostic test results (as seen with some vascular or degenerative diseases of the CNS) or findings incompatible with the clinical history can end up creating a significant challenge for the clinician.
- Running a limited number of investigations aimed at narrowing down the differential list will result in less cost for the owners and less time spent reaching a diagnosis for the clinician.

SYSTEMATIC APPROACH TO LOCALIZING THE LESION

The neurological examination can be divided into two main parts: hands-off examination and hands-on examination.

Hands-off examination

State of consciousness, awareness and behaviour

The first step in the neurological examination should focus on evaluating the animal's state of consciousness, awareness of its environment and response to being handled.

Disturbances of level or quantity of consciousness are classified in order of severity as obtundation, stupor (semicoma) and coma. Stupor and coma both represent a state of unconsciousness. While a stuporous animal can be roused by a painful stimulus, a comatose animal will fail to respond to any environmental stimulus, including pain. As a rule, altered states of consciousness relate to either a diffuse lesion or widespread multifocal lesions of both cerebral hemispheres or a focal lesion affecting the ascending reticular activating system (ARAS) of the brainstem. The latter functions to arouse the cerebral cortex and maintains the state of wakefulness. Acute coma usually results from extensive brainstem lesions or diffuse forebrain lesions secondary to intoxications or a metabolic disorder.

Common changes in quality of awareness and behaviour include disorientation, aggression, vocalizing, circling, compulsive walking or head pressing. Alterations in the patient's level of awareness and behaviour reflect disturbances in the ARAS and limbic system components of the cerebrum or rostral brainstem.

Circling can be caused by a lesion in the vestibular system as well as by an asymmetrical or focal lesion in the forebrain. Tight circles are usually but not exclusively associated with a vestibular disorder, while wide circles are often associated with a forebrain lesion. With vestibular disease, circling is associated with other signs of vestibular dysfunction (head tilt, nystagmus, positional strabismus and/or falling) and is usually ipsilateral to the lesion (except with lesions affecting the caudal cerebellar peduncle, fastigial nucleus and flocculonodular lobes of the cerebellum). Circling is usually towards the side of a focal or asymmetrical forebrain lesion.

Hemi-neglect syndrome, also known as hemi-inattention syndrome, refers to an abnormal behaviour in which an animal with structural forebrain disease ignores sensory input from one half of its environment (e.g. eating from only one half of the food bowl, turning in the wrong direction in response to sound). This syndrome indicates a diencephalic lesion contralateral to the side ignored by the animal.

Posture and body position at rest

The posture and body position at rest should be evaluated and determined as being normal or abnormal. With reference to lesion localization, a number of characteristic abnormal postures can be encountered in the evaluation of the emergency neurology patient:

- **Head tilt.** This abnormal head posture is characterized by a rotation of the median plane of the head along the axis of the body, resulting in one ear being held lower than the other one. A head tilt indicates a vestibular disorder (peripheral or central) and occurs as a result of the loss of antigravity muscle tone on one side of the neck (**2**).
- **Head turn.** Compared with a head tilt, the median plane of the head remains perpendicular to the ground, but the nose is turned to one side (**3**). A head turn is often associated with a body turn (pleurothotonus) and circling. These signs (called adversive syndrome) are usually towards the side of a forebrain lesion.
- **Decerebrate rigidity.** This posture is observed as a result of a rostral brainstem lesion (between the colliculi of the midbrain). It is characterized by rigid extension of all limbs and opisthotonus (extension of the head and neck) associated with a stuporous or comatose mental status (**4**).
- **Decerebellate rigidity.** The rostral part of the cerebellum is inhibitory to the stretch reflex mechanism of antigravity muscles (extensor muscle tone). Lesions at this level can result in opisthotonus, with the forelimbs extended (decerebellate posture). Compared with decerebrate posture, the hips may be flexed by the increased tone in the iliopsoas muscle and mentation remains normal (**5**). This posture is often caused by an acute cerebellar lesion and can sometimes be episodic.
- **Schiff–Sherrington posture.** This posture is observed with an acute severe thoracic or cranial lumbar spinal cord lesion. Such a lesion may interfere with inhibitory ascending neurons that project from the lateral grey matter of the cranial lumbar spinal cord segments cranially to inhibit the forelimb extensor muscles. This posture consists of an extensor hypertonia of the forelimbs, with retention of normal conscious proprioception, voluntary movements and a flaccid paralysis of the hindlimbs (despite the fact that the paralysis is caused by direct interference with the upper motor neuron). This posture is present only in severe and acute lesions, but it does not have prognostic significance.
- **Wide-based stance.** This posture is characteristic of a balance disorder indicating diseases particularly affecting the cerebellum or vestibular apparatus.

Identification of abnormal involuntary movements

- **Myoclonus.** Myoclonus is the clinical sign of sudden contraction followed immediately by relaxation of a specific muscle group. It can be sporadic or repetitive. Sporadic myoclonus can be benign and idiopathic or be a form of simple focal seizure due to a forebrain disorder. Repetitive myoclonus can be constant (often as a result of encephalitis or myelitis caused by distemper virus in dogs), action related (congenital and most commonly caused by a diffuse abnormality of CNS myelination or acquired [e.g. idiopathic generalized tremor syndrome]), postural (head bobber) or episodic (myokymia).
- **Tremor.** With rapid and repeated cycles, repetitive myoclonus demonstrates as a tremor. Tremors can affect all or part of the body and be classified as resting tremors or action-related tremors (also known as kinetic). A resting tremor is present only during rest. An action-related tremor occurs following initiation of voluntary movement. It worsens with increasing levels of activity and disappears with rest. An action-related tremor can be classified in veterinary patients as postural or kinetic.



▲ 2 Left-sided head tilt and facial paralysis in a 6-year-old Boxer with otitis media/interna.



▲ 3 Left-sided head and body turn (pleurothotonus) in a 4-year-old West Highland White Terrier with a left forebrain lesion caused by granulomatous meningoencephalitis.



▲ 4 Decerebrate posture in a 7-month-old Weimaraner with head trauma following a road traffic accident.



▲ 5 Decerebellate posture in a 2-year-old Hungarian Vizsla with a rostral cerebellar artery infarction.

- **Myokymia.** Myokymia is defined as undulating vermiform movements of the overlying skin due to contraction of small bands of muscle fibres.
- **Myotonia.** Myotonia is a sustained repetitive contraction of a muscle or group of muscles without relaxation following physiological stimulus. It occurs in certain congenital and acquired muscle cell membrane disorders.
- **Epileptic seizure.** Epileptic seizures are the clinical manifestation of excessive and/or hypersynchronous electrical activity in the cerebral cortex. They can be focal or generalized. An epileptic seizure refers to a forebrain disorder. Its cause may originate from outside (extracranial causes) or inside (intracranial causes) the brain.

- **Movement disorder.** A movement disorder is defined as an episodic sudden involuntary contraction of a group of skeletal muscles in a conscious patient, with a normal sensorium during the activity. Various terms have been used to describe clinical observations in affected animals (dyskinesia, dystonia, chorea, athetosis, ballism; see Chapter 13).

Evaluation of the gait

Examination of the gait should be done in a place where the patient can be allowed to move freely. This is best accomplished by having the owner walk the animal over a non-slippery surface. If the animal is not making any attempt to walk, body support (e.g. a sling or harness) should be provided as necessary so that any subtle voluntary movement can be detected. A normal gait requires intact function of the brainstem, cerebellum, spinal cord and sensory and motor peripheral nerves, neuromuscular junctions and muscles. The cerebrum's contribution to the gait is less important in dogs and cats when compared with primates.

Evaluation of the gait should be done with the aim of determining if the animal is ataxic, paretic or lame (from either peripheral nerve disease or an orthopaedic disorder) and which limb(s) is/are involved.

Gait generation

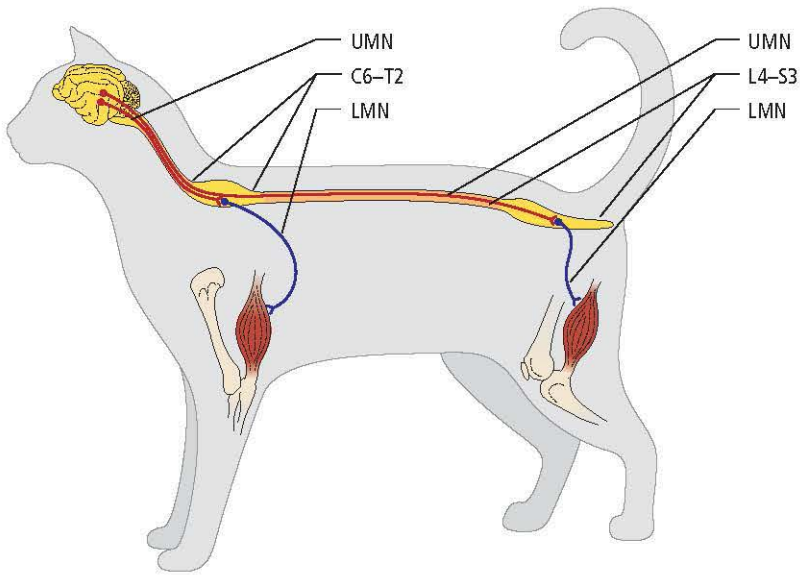
Gait generation requires the interaction between two motor systems: the upper motor neuron (UMN) system and the lower motor neuron (LMN) system (6).

The UMN system is the motor system that is confined to the CNS. It is responsible for the initiation and maintenance of normal movements and for the maintenance of tone in the extensor muscles in order to support the body against gravity. Its cell body lies predominantly within the brainstem. It travels through the brain and/or spinal cord white matter and synapses indirectly (via an interneuron) with an LMN to modulate its activity (essentially via inhibition).

The LMN system is the motor system connecting the CNS with the muscle to be innervated. Its cell body lies within the ventral horn of the spinal cord grey matter or within the cranial nerve nucleus of the brainstem. Its axon leaves the CNS by the ventral nerve roots to join, successively, a spinal nerve and a peripheral nerve before it synapses with an effector muscle. The LMN is the last neuron in the chain of neurons that produces the muscular contraction necessary to maintain posture, support weight and provide the gait (i.e. it is the final common pathway to the effector).

The UMN pathways are responsible for stimulating the appropriate LMN that induces the postural and protraction phases of locomotion.

▼ 6 **Upper motor neuron (UMN) and lower motor neuron (LMN) systems.**



Ataxia

Ataxia is defined as an uncoordinated gait and can arise from either a sensory peripheral nerve or a spinal cord lesion (general proprioceptive ataxia), a vestibular lesion (vestibular ataxia) or a cerebellar lesion (cerebellar ataxia). Ataxia can be further divided into hypometria (shorter protraction phase of gait) or hypermetria (longer protraction phase of gait). General proprioceptive (GP) ataxia reflects the lack of information reaching the CNS responsible for the awareness of the movement and position of the neck, trunk and limbs in space. As a consequence, there may be a delay in the onset of protraction of the limb, which may cause a longer stride than normal. The patient may walk on the dorsal part of its foot or may drag its digits. These signs often overlap with those caused by UMN paresis (see below). Vestibular or cerebellar ataxias are accompanied by other signs of dysfunction of the vestibular apparatus or cerebellum, respectively (see Chapter 9).

Paresis

Paresis is defined as a loss of ability to support weight (LMN disease) or inability to generate a gait (UMN disease) (see *Table 2*). The term paresis implies that some voluntary movement is still present as compared with paralysis, which refers to a more severe paresis (plegia) with complete loss of voluntary movement. Depending on which limbs are affected, the terms paresis/paralysis can be further defined as tetraparesis/plegia (all four limbs affected, caused by a lesion located cranial to T3 spinal cord segment or a generalized LMN disorder), paraparesis/plegia (hindlimbs affected, caused by a lesion caudal to T2), monoparesis/plegia (only one limb affected, caused by a lesion of the LMN innervating the affected limb) and hemiparesis/plegia (limbs on one side affected due to ipsilateral lesion located between T2 and the caudal midbrain or contralateral lesion located in the rostral midbrain) (see Chapter 10).

Based on whether a lesion affects the UMN or LMN system, two types of paresis can be distinguished: UMN paresis and LMN paresis (*Table 2*):

- UMN paresis causes a delay in the onset of protraction (swing phase of the gait), with the resultant stride being longer than normal and with a stiff quality of movement. Lesions of the UMN system typically result in release of the inhibitory effect that the UMN system has on LMNs located caudal to the level of the injury (dysinhibition). This dysinhibition effect is usually more apparent on the extensor muscles, which results clinically in a spastic paresis/paralysis. Lesions at many different levels of the CNS can produce the same set of UMN clinical signs. Due to their close anatomical relationship within the brainstem and spinal cord, most gait abnormalities

Table 2 **Lower motor neuron paresis/upper motor neuron paresis differentiation criteria**

CRITERION	LOWER MOTOR NEURON PARESIS	UPPER MOTOR NEURON PARESIS
Posture	Difficulty supporting weight. Crouched stance as a result of overflexion of the joints	Often normal (unless the animal is paralysed). Abnormal limb position (knuckling, abducted, adducted or crossed over)
Gait	Short strides. Tendency to collapse	Stiff and ataxic strides. Delayed protraction
Motor function	Flaccid paresis/paralysis	Spastic paresis/paralysis
Segmental reflexes	Decreased to absent	Normal to increased
Resting muscle tone	Decreased resistance	Slight resistance
Passive limb flexion/extension	Decreased resistance	Slight resistance
Muscle atrophy	Early and severe neurogenic atrophy	Late and mild disuse atrophy

involving the UMN pathways necessary for gait generation are also associated with some degree of GP ataxia. From a lesion localization point of view, UMN paresis and GP ataxia visible in the gait can occur as a consequence of lesions affecting the brainstem or spinal cord. Apart from lesions caused by peracute disease processes (i.e. infarct, haemorrhage and head trauma), lesions affecting the forebrain cause such a mild contralateral paresis that it is usually not apparent in the gait.

- LMN paresis reflects the degree of difficulty in supporting weight and varies from a short stride, choppy gait to a complete inability to support weight, causing collapse of the limb whenever weight is placed on it. When standing, affected limbs may exhibit a tremor in the muscles. LMN paresis affects the gait with lesions in the peripheral nerves, neuromuscular junction and muscles. Motor deficits observed are ipsilateral to the lesion. Compared with UMN paresis, dysfunction of the LMN does not cause ataxia.

Lameness

Lameness usually presents with a short stride on the affected limb and a long stride on the contralateral limb. Lameness is usually associated with pain from orthopaedic disease. Additionally, it can be associated with nervous system dysfunction referred to as nerve root signature (referred pain down a limb causing lameness or elevation of the limb, resulting from entrapment of the spinal nerve, usually due to a lateralized disc extrusion or nerve root tumour).

Hands-on examination

Postural reaction testing

The primary aim of postural reaction testing is to detect subtle deficits that were not obvious on gait evaluation. In a patient that is recumbent with tetraplegia or paraplegia, evaluation of the postural reactions in the affected limbs is redundant. However, evaluation of the forelimb postural reactions in a paraplegic patient is important in order to detect an abnormality that could suggest a focal cranial thoracic lesion or a multifocal disorder. The postural reactions test the animal's awareness of the precise position and movements of parts of its body, especially the limbs, as well as the animal's ability to generate movement in the part tested.

The postural reactions commonly tested are:

- **The paw replacement reaction**, which is evaluated by placing the paw in an abnormal position (turned over so that the dorsal surface is in contact with the ground) and determining how quickly the animal corrects the paw position (**7**). The majority of the animal's weight should be supported when undertaking this test in order to improve test sensitivity and reduce the interference introduced by orthopaedic disease. Paw replacement reaction can be very difficult to assess in cats that resent having their feet handled. Other postural reaction tests, such as the hopping response, wheel-barrowing and tactile placing, are preferred in this species and should be considered in animals in which the paw replacement reaction is equivocal or difficult to interpret.
- **Hopping response**, which is tested by holding the patient so that the majority of its weight is placed on one limb while the animal is moved laterally (**8**). Normal animals hop on the tested limb in order to accommodate a new body position as their centre of gravity is displaced laterally.
- **Wheel-barrowing**, where the animal's hindlimbs are lifted off the ground by supporting the animal under the abdomen and forcing it to walk forwards (**9**). Abnormal animals may scuff their digits, drag their paws or cross their limbs.



▲ **7** The paw replacement reaction is elicited by gently placing the dorsal part of the foot on the floor. A normal animal should immediately replace its foot in a normal position. This cortically-mediated response tests the conscious awareness of limb position (proprioception).

- **Tactile placing response**, where the animal is lifted and the distal part of the forelimb is brought into contact with the edge of a table. When the dorsal surface of the paw makes contact with the edge of the surface, the animal should immediately place its foot on the surface.

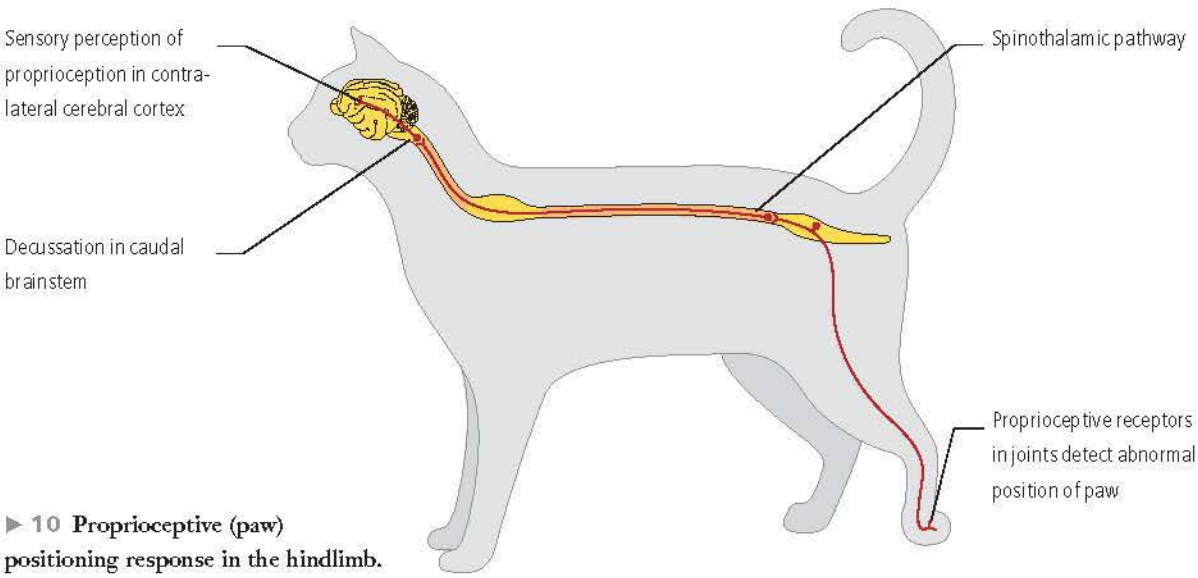
All the components of the peripheral nervous system and CNS that affect the limb tested are needed in order for the animal to perform postural reactions (**10**). These responses are complex in their pathways, but generally involve an afferent arm and an efferent arm. The afferent arm consists of a joint proprioceptor, peripheral sensory



◀ 8 **The normal dog responds to hopping by quickly replacing the limb under the body as it moves laterally. The hopping movement should be smooth and fairly rapid and not irregular or excessive. One forelimb should be carefully compared with the other.**

▼ 9 **Wheel-barrowing is performed with the neck extended and the hindlimbs elevated.**





▶ 10 **Proprioceptive (paw) positioning response in the hindlimb.**

nerve, spinal cord and brainstem ascending pathways, and contralateral forebrain, and the efferent arm involves the contralateral forebrain, descending motor pathways within the brainstem and spinal cord, peripheral motor nerve and skeletal muscle. A lesion affecting any of these components could potentially result in an abnormal postural reaction. Although these reactions are a sensitive test for detecting neurological dysfunction, they do not provide specific information for lesion localization. Their importance in localizing the lesion is dependent on the results of the rest of the neurological examination. In general, postural reactions remain normal in neuromuscular junction and muscle diseases as long as the animal has the strength to support its weight.

Spinal nerve reflexes, muscle mass and tone assessment

Spinal reflexes evaluation should be considered as a continuation of gait evaluation and postural reaction testing and not as a sole entity. Functionally, the spinal cord can be divided into four regions: cranial–cervical (C1–C5); cervicothoracic (C6–T2); thoracolumbar (T3–L3); and lumbosacral (L4–S3). LMN cell bodies are located within the grey matter of the cervicothoracic intumescence (segments C6–T2) for the forelimbs and lumbosacral intumescence (segments L4–S3) for the hindlimbs. Following gait and postural reaction testing, the clinician should be able to narrow down the lesion localization as being cranial to T3 spinal cord segments, caudal to T3 spinal cord segments or within the peripheral nervous system (peripheral nerve, neuromuscular junction or muscles) (see *Table 3*, page 26). Spinal reflexes evaluation helps to narrow down further the lesion localization by testing the integrity of the C6–T2 and L4–S3 intumescences, as well as the respective segmental sensory and motor nerves (LMN) that form the peripheral nerves and the muscles innervated. Spinal reflexes are segmental. They only evaluate the spinal segment(s) within the intumescences corresponding to the stimulated nerve. They do not require normal consciousness. Lesions at the level of these intumescences or affecting the peripheral nervous system result in loss of segmental spinal reflexes as well as reduced muscle tone and mass. Lesions cranial to the intumescence (UMN dysfunction) will result in normal to exaggerated segmental spinal reflexes (due to release of the inhibitory modulatory effect of the UMN on the LMN).

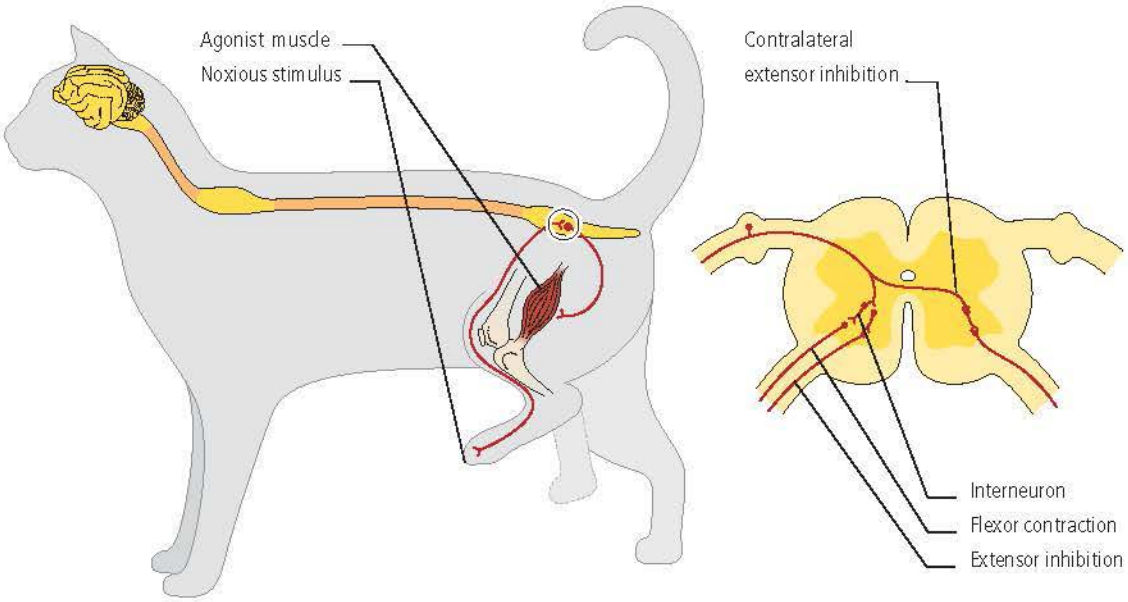
An exception to this rule exists in the context of the emergency patient. Animals with a severe peracute transverse thoracolumbar spinal cord lesion usually show severe hindlimb hypotonia and depressed spinal reflexes for a few days after the onset. Although there is a similar condition in man ('spinal shock'), the reasons for a UMN pathway interruption to cause LMN-like hindlimb signs are poorly understood. Despite many spinal reflexes being described, the most reliable are the withdrawal reflex in the forelimbs and the patellar and withdrawal reflexes in the hindlimbs. Other spinal reflexes are more difficult to perform and to interpret.

Withdrawal (flexor) reflex

A noxious stimulus is applied to the tested limb by pinching the nail bed or digit with fingers or a haemostat. This stimulus causes reflex contraction of the flexor muscles and withdrawal of the tested limb (**11**). If this withdrawal reflex is absent, individual toes can be tested to detect if specific nerve deficits are present. In the forelimb, compression of the digits stimulates nociceptors in the radial nerve dorsally (ulnar nerve in digit five) and in the median or ulnar nerve on the palmar surface. In the hindlimb, compression of digits three to five stimulates nociceptors of the sciatic nerve (peroneal branch dorsally and tibial branch on the plantar surface).



▲ **11** **A normal withdrawal reflex in the hindlimb implies flexion of the hock, stifle and hip. This should normally be performed with the animal in lateral recumbency; however, in some animals it is possible to perform this test only when they are standing and minimally restrained.**



▲ **12** **Withdrawal (flexor) reflex. When a noxious stimulus is applied to a digit, the limb should be withdrawn towards the body. Sensory input enters the spinal cord through the dorsal root to activate ipsilateral flexor motor neurons via interneurons and simultaneously inhibit the antagonist extensor muscles.**



▶ **13** **The patellar reflex is elicited by hitting the patellar tendon with a reflex hammer and observing a reflex extension of the stifle joint.**

The withdrawal reflex is a segmental spinal cord reflex that only depends on the function of the local spinal cord segments (**12**). In the forelimb it evaluates the integrity of the spinal cord segments C6–T2 (and associated nerve roots), the brachial plexus, the peripheral nerves (radial, axillary, musculocutaneous, median and ulnar nerves) and the muscles innervated. In the hindlimbs it evaluates the integrity of the spinal cord segments L4–S1 (and associated nerve roots), the femoral and sciatic nerves and the muscles innervated. It should be stressed that the withdrawal reflex in the fore- or hindlimbs does not depend on the animal's nociception (perception of a noxious stimulus).

Patellar reflex

The patellar reflex is elicited by hitting the patellar tendon and observing a reflex contraction of the quadriceps muscle and extension of the stifle joint (**13**). It is performed when the dog is in lateral recumbency, with the stifle slightly flexed and the tested limb supported by placing one hand under the thigh. It is best performed in cats with the cat in dorsal recumbency between the thighs of the examiner. This position allows the stifle to be slightly flexed and a comparison to be made between the two sides.

The patellar reflex evaluates the integrity of spinal cord segments L4–L6 (and associated nerve roots) as well as the femoral nerve. A weak or absent reflex indicates a

Table 3 **Determination of an anatomical diagnosis based on gait, postural reactions and segmental spinal reflex evaluation**

LIMB(S) PRESENTING WITH ABNORMAL GAIT AND/OR ABNORMAL POSTURAL REACTIONS	SEGMENTAL SPINAL REFLEXES IN AFFECTED LIMB	LIKELY ANATOMICAL DIAGNOSIS
All four limbs	Normal to increased all four limbs	Brainstem or (C1–C5) spinal cord segments
	Decreased to absent all four limbs	Generalized polyneuropathy/ junctionopathy/myopathy
	Decreased to absent forelimbs and normal to increased hindlimbs	(C6–T2) spinal cord segments
Bilateral hindlimbs	Normal to increased	(T3–L3) spinal cord segments
	Decreased to absent	(L4–S3) spinal cord segments, peripheral nerve roots/nerve of the hindlimbs
Fore- and hindlimbs on the same side of the body	Normal to increased fore- and hindlimbs	Ipsilateral brainstem or (C1–C5) spinal cord segments
	Decreased to absent forelimbs and normal to increased hindlimbs	Ipsilateral (C6–T2) spinal cord segments
Unilateral forelimb	Normal to increased	Ipsilateral brainstem or (C1–C5) spinal cord segments
	Decreased to absent	Ipsilateral (C6–T2) spinal cord segments or in that limb affecting either the nerve roots, brachial plexus or peripheral nerves
Unilateral hindlimb	Normal to increased	Ipsilateral (T3–L3) spinal cord segments
	Decreased to absent	Ipsilateral (L4–S3) spinal cord segments or in that limb affecting either the nerve roots or peripheral nerves

lesion of the L4–L6 spinal cord segments or the femoral nerve. A similarly weak or absent reflex can on occasion be seen with stifle disease. A lesion cranial to the L4 spinal cord segment can cause a normal or exaggerated patellar reflex. In the absence of other neurological deficits, an exaggerated patellar reflex means little and can be observed in an excited or nervous animal. Evaluation of the extensor tone of the hindlimb can be used as a control in animals with an ambiguous patellar reflex, as it involves the same neuroanatomical components (L4–L6 spinal cord segments, femoral nerve and quadriceps muscle). Finally, the patellar reflex can appear hyperreflexic with a sciatic nerve or L6–S2 spinal cord segment lesion. This pseudohyperreflexia is a result of decreased tone in the muscles that flex the stifle and normally counteract stifle extension during the patellar reflex.

Perineal reflex

The perineal reflex is elicited by stimulation of the perineum with a haemostat, resulting in contraction of the anal sphincter and flexion of the tail.

This reflex tests the integrity of caudal nerves of the tail, the pudendal nerve, spinal cord segments S1 to Cd5 and associated nerve roots.

Cutaneous trunci (panniculus) reflex

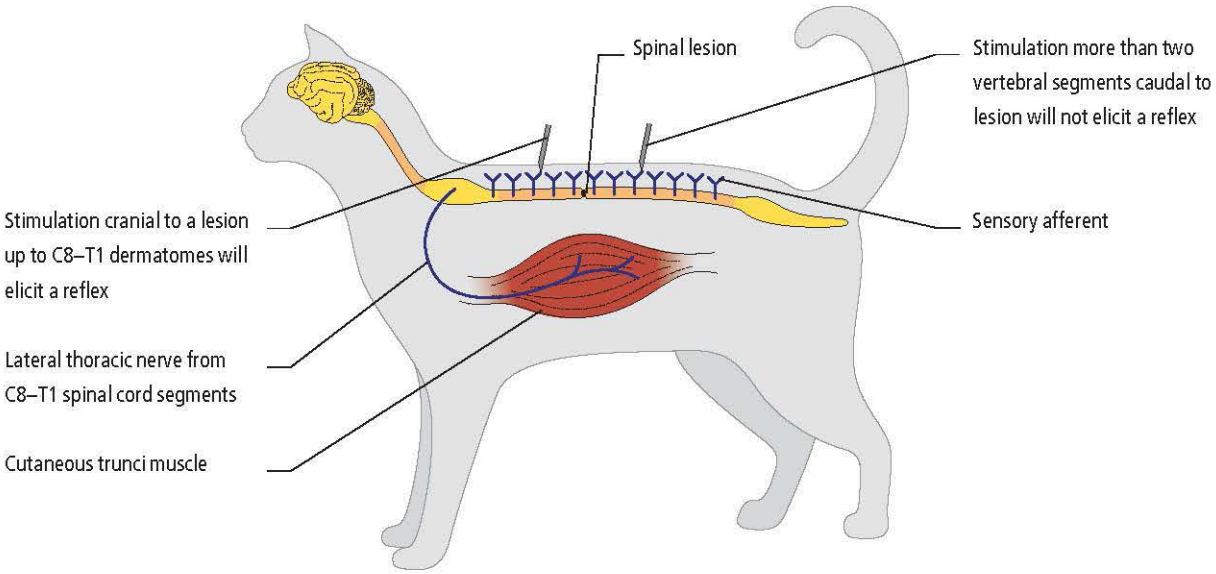
This reflex is elicited by pinching the dorsal skin of the trunk on either side of the dorsal spinous processes between the vertebral level T2 and L4 to L5 and observing a contraction of the cutaneous trunci muscle bilaterally producing a twitch of the overlying skin. This reflex is present in the thoracolumbar region and is absent in the neck and sacral regions. Testing is started at the level of the ilial wings. If the reflex is present at this level, the entire pathway is intact and further testing is not necessary.

From the dermatome tested, the sensory nerve from the skin enters the spinal cord at the level of the segment corresponding to that dermatome (approximately two vertebrae cranial to the level tested) (**14**). Afferent sensory information ascends the spinal cord and synapses bilaterally at the C8–T1 spinal cord segments with the motor neurons of the lateral thoracic nerve, which courses through the brachial plexus and innervates the cutaneous trunci muscle. The panniculus reflex can be decreased or lost with a lesion anywhere in this pathway (dorsal nerve roots, spinal cord, lateral thoracic nerve). With spinal cord lesions, this reflex is lost caudal to the spinal cord segment affected, indicating the presence of a transverse myelopathy. Pinching the skin cranial to the lesion results in a normal reflex, while stimulation of the skin caudal to the lesion does not elicit any reflex. Such findings help to further localize lesions between T3 and L3. This reflex can also be lost ipsilaterally (with normal reflex on the other side) with conditions affecting the brachial plexus, regardless of the level that the skin is stimulated. In the absence of other neurological deficits, the absence of the cutaneous trunci reflex means little.

Nociceptive testing

Although it only defines the degree of dysfunction and not the degree of structural damage, nociceptive testing has significant prognostic value in cases of spinal cord or peripheral nerve lesions. The purpose of this test is to detect and map out any areas of sensory loss. This may help in identification of specific peripheral nerves, nerve roots and spinal cord segments involved in the disease process. Assessment of pain sensation requires a noxious stimulus and evaluation of the animal's response. If an area of diminished or absent nociception is encountered, its boundaries should be demarcated to see whether it has a segmental or peripheral nerve distribution and whether it is absent below a certain level of the trunk.

▼ **14 Schematic representation of the neurological pathways responsible for the cutaneous trunci reflex.**



Nociception is commonly tested by pinching the digits with the fingers or with haemostats. If no response is elicited when using fingers, the test should be repeated with haemostats to confirm that the response is absent. Other areas of cutaneous sensory testing include the tail, perineum and perianal region, as well as cutaneous sensory distribution of the fore- and hindlimb nerves (see Chapter 16).

Only a behavioural response to noxious stimulus (turning of the head, attempt to bite) indicates conscious pain perception (**15**). Withdrawal of the limb is only the flexor reflex and should not be taken as evidence of nociception.

Cranial nerve examination

Cranial nerve (CN) examination can be performed individually and sequentially from CN I to CN XII, or by more of a regional approach (*Table 4*). The latter method is more appropriate to the evaluation of the emergency neurology patient. Testing of these nerves should be done in conjunction with the assessment of mentation, gait, postural reaction and segmental spinal reflexes to determine whether there is brainstem disease versus peripheral CN disease.

Vision, pupil size and response

Menace response

The menace response is elicited by making a threatening gesture at the eye tested (**16**). The expected response is closure of the eyelids. The contralateral eye must be blindfolded with the other hand in order to assess each eye separately. Care must be taken not to touch the eyelashes or to create air currents that might stimulate sensation of the face (CN V; trigeminal nerve), which could elicit a palpebral or corneal reflex (see below).

This reaction is a learned response that may not be developed until 10–12 weeks of age in puppies and kittens. The afferent arc of this response involves three neurons:

- The first neuron in this arc is the bipolar cell of the retina. This receives impulses from the neuroepithelial cells of the retina (rods and cones).
- The second afferent neuron is the ganglion cell of the retina. Its axons lie in the optic nerve (CN II) and continue through the optic chiasm and proximal part of the optic tract on the opposite side to the eye being menaced.
- This second neuron synapses with neuron three in the lateral geniculate nucleus. The axons then project to the visual cortex (mostly occipital cortex) in a band of fibres called the optic radiation.



▲ **15** Nociception is tested by pinching the digits with the fingers or with haemostats and observing a behavioural response to the noxious stimulus (turning of the head, as in this picture, vocalization and/or an attempt to bite).



▲ **16** The menace response is elicited by making a threatening gesture at the eye. The expected response is closure of the eyelids. The contralateral eye should be blindfolded with the other hand to assess each eye separately.

Table 4 **Cranial nerve examination**

CRANIAL NERVE TEST	AFFERENT CRANIAL NERVE	BRAIN REGION	EFFERENT CRANIAL NERVE	PRINCIPAL EFFECT NOTED
Menace response	CN II – optic	Forebrain, cerebellum, brainstem	CN VII – facial	Blink elicited by a menacing gesture
Visual placing	CN II – optic	Forebrain	None	Reach out for support on approaching the table
Pupillary light reflex	CN II – optic	Brainstem	CN III – oculomotor	Pupillary constriction elicited by shining a light in the eye
Dark adaptation test	CN II – optic	Hypothalamus, brainstem	Sympathetic supply to the eye	Pupillary dilation in darkness
Palpebral reflex	CN V – trigeminal (ophthalmic or maxillary)	Brainstem	CN VII – facial	Blink elicited by touching of the medial or lateral canthus of the eye
Corneal reflex	CN V – trigeminal (ophthalmic)	Brainstem	CN VII – facial; CN VI – abducens	Blink and globe retraction elicited by touching the cornea
Response to nasal stimulation	CN V – trigeminal (maxillary and ophthalmic)	Forebrain, brainstem	None	Withdrawal of the head elicited by touching the nostril
Oculovestibular reflex	CN VIII – vestibular	Brainstem	CN III – oculomotor; CN IV – trochlear; CN VI – abducens	Nystagmus induced by moving the head
Gag reflex	CN IX – glossopharyngeal; CN X – vagus	Brainstem	CN IX – glossopharyngeal; CN X – vagus	Contraction of the pharynx elicited by palpating the pharynx

The efferent arc of this response is not well understood. The information generated in the occipital cortex (contralateral to the eye stimulated) is forwarded to the motor cortex via association fibres. The corticobulbar pathways to the facial nerve nucleus (CN VII) then transmit the motor information. This response requires intact facial nerve function. This function should be separately evaluated with the palpebral reflex (see below). There is some experimental and clinical evidence for cerebellar involvement in the menace response efferent pathways. Unilateral cerebellar lesions can lead to an ipsilateral menace response loss with retention of normal vision. The neuronal pathways through the cerebellum are, however, not known.

Visual placing response

This placing reaction is tested by carrying a small dog or a cat under its chest towards a table edge, but without letting the forelimbs touch the table. On approaching the surface the animal will reach out to support itself on the table. Each eye can be tested separately by covering the eye contralateral to the one being tested.

This response requires intact visual pathways, mentation and postural control of the forelimbs. It can be used to assess visual function in an animal where the menace response is ambiguous.

Evaluation of pupil size

Immediately after menace response testing, the pupil's size and response to light and darkness should be evaluated. Pupillary abnormalities are common following intracranial trauma or vascular compromise. The size of the pupils represents a balance of the parasympathetic system (responsive to the amount of light entering the eye) and the sympathetic system (responsive to the emotional state of the animal). The pupil regulates the amount of light reaching the retina through the parasympathetic nerve pathways that innervate the iris. The parasympathetic component of the oculomotor nerve (CN III) is involved in the control of pupillary constriction, while the somatic efferent component of the oculomotor nerve controls the motor innervation of the levator palpebrae superioris (elevation of the upper eyelid) ipsilateral dorsal, ventral and medial recti extraocular muscles, as well as the ventral oblique muscle (movement of the eyeball). The tone of the iris dilator muscle is maintained by the sympathetic system, which keeps the pupil partially dilated under normal conditions and dilates it more notably during periods of stress, fear and painful stimuli. The ocular sympathetic nervous system also innervates and provides tone to the smooth muscle of the periorbita and eyelids. This tone keeps the eyeball protruded, the palpebral fissure widened and the third eyelid retracted.

Assessment of pupillary size and equality should be determined in ambient light as well as in darkness. Normally, the pupils should be symmetrically shaped and equal to each other in size. Animals with pupils of unequal size (anisocoria) or shape (dyscoria) must be found free of primary or secondary anatomical or mechanical ocular abnormalities (iris atrophy, uveitis or glaucoma) before consideration is given to a neurological dysfunction. Determining which pupil is abnormal is achieved by checking the pupillary light reflex (PLR) and determining if the asymmetry in pupil size increases in bright light or in complete darkness (dark adaptation test).

Pupillary light reflex

The PLR is tested by shining a bright light into the pupil and assessing for pupillary constriction (direct reflex). The opposite pupil should constrict at the same time (consensual or indirect reflex). A slight dilation usually follows the initial pupillary constriction (pupillary escape) as a consequence of light adaptation of photoreceptors.

The PLR involves an afferent arm and an efferent arm. The afferent arm of this reflex shares some common pathways (ipsilateral retina, optic nerve, optic chiasm and contralateral optic tract) with part of the afferent arm of the menace response and visual placing. These tests use different integration centres within the brain and different efferent pathways. The PLR does not test the animal's vision and the cerebrum is not involved in the PLR pathway. The efferent arm of the PLR reflex is mediated by the parasympathetic portion of CN III. While axons involved in vision reach the conscious level after synapse with the lateral geniculate nucleus, the axons involved in the PLR synapse with a third neuron in the pretectal nucleus. Most of the axons arising from this nucleus decussate again and synapse on the parasympathetic component of the oculomotor nucleus (ipsilateral to the stimulated eye) in the mesencephalon. There are also neurons that do not decussate and which project to the oculomotor nucleus on the contralateral side of the stimulated eye. The proportion of axons that decussate is higher than that of the ones that do not decussate, explaining why the direct response (constriction in the eye receiving the light stimulus) is greater than the consensual response (constriction in the eye not receiving the light stimulus). Combining the results of the menace response, visual placing and PLR tests helps to localize the lesion as being within the common pathways or not (see Chapter 12).

In the dark adaptation test the eyes are dark adapted in complete darkness for a couple of minutes in order to allow complete relaxation of the pupillary sphincter muscle.

Trigeminal and facial nerve functions

The trigeminal nerve (CN V) provides sensory innervation of the face (cutaneous elements of the face as well as the cornea, mucosa of the nasal septum and mucosa of the oral cavity) and motor innervation to the masticatory muscles (temporalis, masseter, medial and lateral pterygoid and rostral part of the digastric muscles). The motor function of CN V is assessed by evaluating the size and symmetry of the masticatory muscles and testing the resistance of the jaws when opening the mouth.

The sensory function (sensation of the face) can be individually tested by the corneal reflex (ophthalmic branch) and the palpebral reflex (ophthalmic or maxillary branch when touching the medial or lateral canthus of

the eye, respectively) (**17**), by pinching the skin of the face with haemostat forceps and observing an ipsilateral blink or facial twitch, and by the response to nasal stimulation. As for the menace response, the response to nasal stimulation requires an intact contralateral forebrain. One of the two nostrils is stimulated using a pair of forceps or a pen, while the animal's eyes are masked to prevent any visual input. The afferent arc involves the sensory component of the trigeminal nerve (ophthalmic and maxillary branch of CN V), which conducts the information to the brainstem where it is continued to the contralateral forebrain. The expected response is a withdrawal movement of the head and neck (**18**). As with the menace response, this response might be abnormal in the presence of a structural contralateral forebrain lesion.

The facial nerve (CN VII) is motor to the muscles of facial expression and sensory (providing the sense of taste) to the rostral two-thirds of the tongue and palate. Its parasympathetic component innervates the lacrimal glands and the mandibular and sublingual salivary glands. The motor function of CN VII is primarily assessed by observation of the face for movement of the ears, eyelids, lips and nostrils and for symmetry of the lips. The facial nerve is also the motor efferent part of the following tests:

- Palpebral reflex (CNs V and VII).
- Corneal reflex (CNs V and VII).
- Menace response (CNs II and VII).
- Pinching of the face (CNs V and VII).

The Schirmer tear test helps to evaluate the parasympathetic supply of the lacrimal gland associated with CN VII. Examining the mouth for a moist mucosa can subjectively assess salivation.

Eye movement and position

Observation of the animal's body and head posture at rest and evaluation of its gait can provide a lot of information about the vestibular function of CN VIII (see Chapter 14). This function can also be more specifically assessed by testing the oculovestibular reflex and looking for pathological nystagmus. Nystagmus is an involuntary rhythmic movement of the eyeballs. Physiological (or vestibular) nystagmus is a nystagmus that occurs in normal animals, while pathological nystagmus reflects an underlying vestibular disorder. In both instances the nystagmus has a slow and fast phase (i.e. jerk nystagmus). A physiological nystagmus can be induced in normal individuals by rotation of the head from side to side (oculovestibular reflex). The test is best performed on a



▲ **17** The palpebral reflex is elicited by touching the medial or lateral canthus of the eye and observing a reflex closure of the eyelids. The afferent arm of this reflex is mediated by the trigeminal nerve (CN V sensory), while the efferent arm is mediated by the facial nerve (CN VII).



▲ **18** The response to stimulation of the nasal mucosa is a cortically mediated withdrawal of the head. The afferent arm is mediated by the trigeminal nerve (CN V sensory). The integration of this response occurs in the contralateral forebrain.

cat or a small dog by holding the animal at arm's length and rotating it from side to side; nystagmus may only be seen at the end of the movement. Physiological nystagmus stabilizes images on the retina during head movement. It is always observed in the plane of rotation of the head and consists of a slow phase in the direction opposite to that of the head rotation and a fast phase in the same direction as the head rotation. In the absence of any head movement, nystagmus should never be present in a normal animal.

Two types of pathological nystagmus can be observed with vestibular dysfunction. It can be spontaneous (observed when the head is in a normal position at rest) and/or positional, which occurs when the head is held in different positions (for example to either side, dorsally or by placing the animal upside down on its back). Nystagmus is usually classified on the basis of its direction (the fast movement) and may be horizontal, vertical or rotatory. With disorders of the peripheral components of the vestibular system in the inner ear, the direction of the nystagmus is always opposite to the side of the lesion and is usually horizontal or rotatory. Lesions of the central components of the vestibular system can cause pathological nystagmus in any direction and occasionally it changes direction with different head positions. A vertical nystagmus is more commonly due to a central lesion.

Strabismus refers to an abnormal position of the eyeball within the orbit. While examining the eyes, the eyeballs should be assessed as to whether they are normally positioned in the orbits. Normal position of the eyeball is dependent on the innervation of the extraocular muscles by the oculomotor (CN III), trochlear (CN IV) and abducens (CN VI) nerves. The function of these CNs can be tested during the oculovestibular reflex, evaluating the degree of abduction (CN VI) and adduction (CN III). Strabismus can be seen with vestibular dysfunction when the head is placed in an abnormal position (extended dorsally or the animal placed upside down on its back). Vestibular dysfunction often causes a ventral or ventrolateral positional strabismus in the eye on the same side as the vestibular lesion.

Laryngeal, pharyngeal and tongue function

Because of their proximity in the brainstem, the glossopharyngeal (CN IX) and vagus (CN X) nerves share sensory (nucleus solitarius) and motor (nucleus ambiguus) nuclei. CN IX innervates the musculature of the pharynx and palatine structures. It provides sensory innervation to the caudal third of the tongue and pharyngeal mucosa (taste). Its parasympathetic component innervates the parotid and zygomatic salivary glands. CN X controls motor function of the larynx (recurrent laryngeal branch), pharynx and oesophagus (cervical oesophagus innervated by the pharyngeal and recurrent laryngeal branches; thoracic oesophagus innervated by the vagal branches). It provides sensory function to the larynx, the pharynx and the thoracic and abdominal viscera. Its parasympathetic component provides innervations to all the thoracic and abdominal viscera, except those of the pelvic region.

The pharyngeal reflex can assess CN IX and X function. This reflex is also known as the swallowing or gag reflex. It is evaluated by applying external pressure to the hyoid bones to stimulate swallowing or by stimulating the pharynx with a finger to elicit a gag reflex. It can also be evaluated by watching the animal eat and/or drink and by opening the mouth wide: the animal will usually close its mouth, swallow and lick its nose, allowing simultaneous evaluation of the tongue. The parasympathetic innervation of CN X can be evaluated by testing the oculocardiac reflex. This is achieved by applying digital pressure to both eyeballs and observing simultaneously a reflex bradycardia (mediated as well by CN V).

CN IX dysfunction results in dysphagia, an absent gag reflex and reduced pharyngeal tone. Animals frequently cough after drinking and swallow repeatedly because of an accumulation of saliva in their pharynx. CN X dysfunction abnormalities include dysphagia, inspiratory dyspnoea (due to laryngeal paralysis), voice changes and regurgitation (due to megaoesophagus if there is a bilateral vagal disorder). The pharyngeal and oculocardiac reflexes are absent.

CN XII provides motor innervation to the muscles of the tongue. The nucleus is in the caudal medulla and can therefore be affected by high cervical lesions. The nerve exits the skull via the hypoglossal foramen. CN XII function can be evaluated by inspecting the tongue for atrophy, asymmetry or deviation to one side. Manually stretching the tongue and observing a voluntary retraction helps assess the tongue's tone. Applying food 'paste' to the nose and observing the animal licking can assess its movement. Lesions affecting CN XII can result in problems with prehension, mastication and deglutition. With unilateral and recent lesions, the tongue tends to deviate towards the contralateral side. With unilateral and chronic lesions, the tongue protrudes towards the side of the lesion and atrophy is observed ipsilaterally. Muscle fasciculations may be obvious on the affected side in the denervated tongue.

Palpation

Palpation and manipulation to detect painful areas and/or restricted movement are usually performed last in order to avoid losing the cooperation of the patient.

Head

The head must be palpated to detect any asymmetry, focus of pain or persistence of the fontanelles.

Spine

Palpation of the spine starts by applying gentle downward pressure on the spinous process and then along the transverse processes. The degree of pressure applied should be progressively increased. The presence of spinal hyperaesthesia or deformity should be noted.

Limbs

Palpation of the limbs is indicated to evaluate the animal for musculoskeletal conditions that can mimic a neurological disorder. The joints should be carefully palpated for evidence of swelling, pain or instability. Palpation of the muscular system can help to detect focal muscle atrophy. Such findings could indicate disease in the spinal cord segment, nerve root or peripheral nerve that innervates a specific muscle (LMN dysfunction), or they could be related to disuse atrophy associated with an orthopaedic condition.

HOW TO ESTABLISH A DIFFERENTIAL DIAGNOSIS LIST

The differential diagnosis list is dependent on the anatomical diagnosis. Compiling a differential diagnosis list is essential in choosing and interpreting any diagnostic test however sophisticated it may be. The aim of performing such diagnostic tests should be only to confirm or exclude the differentials in the list and not replace the clinical evaluation. The differential diagnosis list should be developed taking into account:

- Signalment.
- Historical data. Questioning of the owner should be aimed at defining the mode of onset (acute, subacute, chronic or episodic) and evolution of the condition. Furthermore, historical data can give clues as to how widespread or focal the disease process is in the nervous system, whether there was evidence of asymmetry, and how severe the signs have been.
- Neurological findings. The aim of the neurological evaluation is to define the lesion localization (forebrain, brainstem, cerebellum, spinal cord segment, peripheral nerve, neuromuscular junction and muscle) and distribution of the disease (focal, multifocal, diffuse) within the nervous system.

Disease processes that can affect the nervous system can be classified according to the mnemonic 'VITAMIN D' (Vascular–Inflammatory/Infectious–Traumatic/Toxic–Anomalous–Metabolic–Idiopathic–Neoplastic–Nutritional–Degenerative). Each of these disease processes has a typical signalment, onset and progression, as well as distribution within the nervous system (see *Table 5*, next page). In the context of the neurology emergency patient, the mnemonic can be abbreviated to 'VITIMN' (Vascular–Inflammatory/Infectious–Traumatic/Toxic–Idiopathic–Metabolic–Neoplastic), as it is unlikely (although not impossible) that the other disease processes (Anomalous, Nutritional, Degenerative) will have an acute presentation.

Table 5 **Disease processes classified according to the mnemonic 'VITAMIN D'**

PATHOLOGICAL PROCESS	MODE OF ONSET	EVOLUTION	DISTRIBUTION
Vascular	Peracute or acute (haemorrhage may cause subacute onset)	Non-progressive or regressive (haemorrhage may cause progression over a very short period)	Focal and often asymmetrical
Inflammatory/infectious	Acute, subacute or insidious	Progressive (wax and wane in some cases early after onset)	Focal or multifocal. Asymmetrical or symmetrical
Traumatic	Peracute or acute	Static or improve over time	Often focal. Asymmetrical or symmetrical
Toxic	Acute	Variable	Diffuse and bilaterally symmetrical
Anomalous	Chronic (occasionally acute)	Non-progressive or slowly progressive, usually early in life	Variable
Metabolic	Variable (often acute)	Wax and wane or progressive	Diffuse and bilaterally symmetrical
Idiopathic	Acute	Non-progressive or regressive	Specific to each syndrome
Neoplastic	Chronic (occasionally acute)	Progressive	Often focal. Asymmetrical or symmetrical
Nutritional	Variable (acute or insidious)	Progressive	Diffuse and bilaterally symmetrical
Degenerative	Chronic	Progressive	Often diffuse and symmetrical

WHAT DO DO NEXT?

With a clear knowledge of the region of the nervous system involved and the differential list reduced to no more than three or four disease processes, consideration should only be given to diagnostic tests that help to further narrow down the list and can be afforded by the client. The least invasive tests should be performed first.

RESPIRATORY AND CARDIOVASCULAR SUPPORT

Anthea Raisis & Gabrielle Musk

INTRODUCTION

Maintenance of normal oxygenation, ventilation and perfusion (the ABC of resuscitation) is essential in the neurological patient to prevent secondary neurological injury or exacerbation of the underlying condition. In addition, correction of hypoxaemia, hypercapnia and poor perfusion are the most important strategies for reducing intracranial pressure (ICP). The type and extent of supportive care required will depend on the cause of respiratory and/or cardiovascular impairment and the severity of disruption to normal oxygenation, ventilation and perfusion. Techniques for maintaining normal respiratory and cardiovascular function and, therefore, adequate oxygen delivery to the tissues are outlined in this chapter.

PROVIDING AN ARTIFICIAL AIRWAY

The indications for providing an artificial airway are listed below:

- Laryngeal paresis or paralysis, which can be caused by cranial nerve deficits associated with disorders of the brainstem or generalized neuromuscular disease.
- Laryngeal spasm (e.g. tetanus).
- An inability to protect the airway adequately (e.g. severe depression/recumbency associated with intracranial disease).
- Mechanical ventilation.

Treatment methods for acquiring and maintaining a patent airway

Oral endotracheal intubation

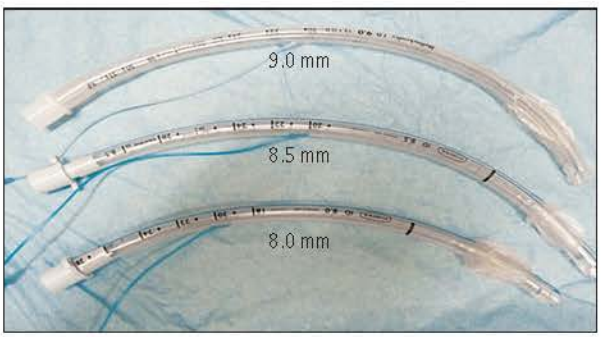
Specific indications

- Emergency management of upper airway obstruction (e.g. laryngeal spasm, laryngeal paralysis).
- Protection of airway in an obtunded/unconscious animal.
- Animals that need mechanical ventilatory support.

Precautions

Oral endotracheal intubation in most animals will require sedation or anaesthesia. Details of how to sedate/anaesthetize a neurological patient safely are described in Chapter 29.

Selection of an appropriately sized endotracheal tube (ETT) is essential (**19**). Resistance to breathing is markedly increased as the diameter of the ETT decreases. If the diameter of the tube is halved, resistance increases 16-fold. To minimize resistance to breathing, the largest diameter tube that can be easily and safely passed should be used. If the ETT is too long, resistance to expiration will also increase (doubling the length will double the resistance to flow) and the risk of excessive



▶ 19 Selection of an appropriate endotracheal tube for each animal is required to ensure that resistance to breathing is not excessive. When preparing for intubation, select the most appropriate endotracheal tube size in addition to tubes 0.5–1.0 mm above and below that size as shown here.

equipment dead space or inadvertent endobronchial intubation increases (**20**).

The increased work of breathing associated with increased resistance can be overcome by mechanical ventilation. The potential for this increased work to reduce the adequacy of ventilation and cause hypercapnia will be greatest in any animal expected to breathe spontaneously or when attempting to wean an animal off the ventilator. An excessively long ETT will also increase the apparatus dead space, leading to rebreathing of expired carbon dioxide (CO_2). This also increases the risk of hypercapnia and increased ICP in the neurological patient.

As oral intubation bypasses the nasal cavity, which normally humidifies inspired air, the airways are predisposed to desiccation. Humidification of gases is essential to minimize drying of lower airways and should always be used in patients that are ventilated for anything other than a short period of time.

Inflation of the ETT cuff is required to prevent aspiration of saliva or gastric contents. The cuff should be inflated just enough to create a seal. If excessive or prolonged inflation pressure is created, the risk of pressure necrosis of the tracheal mucosa increases. The pressure of the small arterioles in the tracheal mucosa is very low, so the pressure within the cuff should not exceed 25 mmHg. Careful inflation of the cuff is required to minimize damage to the mucosa. During prolonged intubation, occasional repositioning of the endotracheal tube may help reduce mucosal ischaemia; however, repositioning the ETT increases the risk of aspiration of secretions that have accumulated above the cuff. If the tube is repositioned, the pharynx and oesophagus should be suctioned prior to cuff deflation to reduce the risk of secretions entering the airway.

Tracheostomy

Specific indications

- Chronic management of airway dysfunction in conscious patients (e.g. animals with tetanus, laryngeal paresis).
- To reduce the amount of sedation/anaesthesia required to immobilize animals requiring mechanical ventilation.
- Severe laryngeal trauma.

Precautions

The tracheostomy tube must be secured adequately in place to prevent accidental removal and loss of the airway. It is essential that the tube can still be removed rapidly should obstruction occur. Tying the tube in place is preferred over suturing (**21**).



▲ **20** Endotracheal tubes and other apparatus (such as the capnograph sampling connector; arrow) extending beyond the level of the animal's incisors may increase apparatus dead space, resistance to expiration and the work of breathing. Always pre-measure the endotracheal tube before placement.



▲ **21** A tracheostomy tube is used to provide a patent airway in animals with severe compromise of the upper respiratory tract. The tube should be tied in place (arrow) to allow rapid removal should obstruction of the tube occur.

The accumulation of secretions may occlude the tube. When mechanical ventilation is not required and the risk of aspiration is considered minimal, it is recommended that an uncuffed tube is used (**22**). It is also recommended that the diameter of the tube is one half the diameter of the trachea, so the animal can breathe around the tube for short periods should the tube become occluded.

Care of the tracheostomy site is labour intensive. Animals need constant monitoring, as occlusion of the tube can result in death within minutes. Regular suctioning is required to prevent accumulation of secretions. The tube should be replaced 1–2 times a day.

Intratracheal catheter

If the upper airway is completely obstructed, an intratracheal catheter or needle (large dog: 16 g; small to medium dog: 18 g) can be placed (**23**). Oxygen can be insufflated via these catheters/needles for <5 minutes.

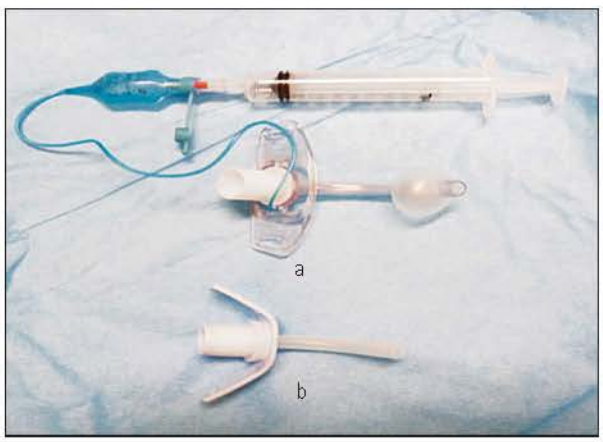
Specific indications

- Obstructed airway and impending respiratory arrest.
- Short-term oxygenation while oral intubation or tracheostomy is performed.

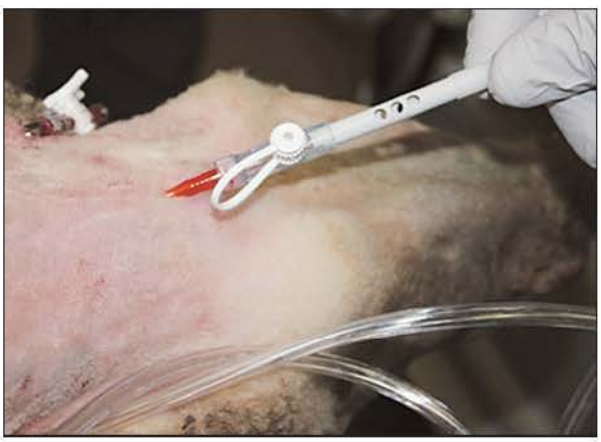
Precautions

This method of oxygenation is for short-term use only (<5 minutes) and must be used with conservative oxygen flow rates. When the airway is completely obstructed, oxygen insufflated into the lung via a narrow needle or catheter cannot be expired, therefore there is a risk of rupturing the lung, resulting in a pneumothorax. To determine suitable flow rates, the volume of the animal's lungs must be considered. For example: a 20 kg dog would have an approximate tidal volume of 200 ml (based on 10 ml/kg). Therefore, an oxygen flow of 1 litre minute^{-1} would fill the tidal volume of the lungs in 12 seconds, while an oxygen flow rate of 200 ml/minute would take 1 minute.

This method does not allow for mechanical ventilation of the animal, and hypercapnia will occur. Intubation should be performed promptly and mechanical ventilation instigated as soon as a patent airway is available.



▲ **22** A cuffed tracheostomy tube (a) is required when mechanical ventilation is being performed. However, when the animal is conscious and spontaneously breathing, an uncuffed tracheostomy tube (b) is preferred.



▲ **23** An intratracheal catheter, as shown here, can be used to provide short-term (<5 minutes) oxygen supplementation in animals that are completely obstructed.

BREATHING

Adequate oxygenation (arterial oxygen partial pressure [PaO_2] ≥80 mmHg [10.7 kPa]; saturation of haemoglobin with oxygen [SpO_2] ≥95%) and ventilation (arterial carbon dioxide partial pressure [$PaCO_2$] 35–40 mmHg [4.7–5.3 kPa]; end-tidal carbon dioxide partial pressure [$P'ETCO_2$] 30–35 mmHg [4–4.7 kPa]) are required to maintain cerebral oxygen delivery and prevent increases in ICP.

Oxygen supplementation

Indications

Oxygen supplementation is indicated if there is a critical decrease in oxygen delivery to the brain. Oxygen delivery (DO_2) is a product of cardiac output (CO) and oxygen carrying capacity (CaO_2) measured as the oxygen content of arterial blood:

$$DO_2 = CO \times CaO_2$$

The oxygen content of arterial blood is a combination of oxygen bound to haemoglobin (haemoglobin × SpO_2 × 1.34) and that dissolved in the plasma (0.003 × PaO_2). As the majority of oxygen is carried in the blood bound to haemoglobin, decreases in oxyhaemoglobin saturation and haemoglobin concentration have the greatest influence on oxygen delivery to tissues, including the brain. Decreases in oxygen saturation of haemoglobin may occur due to decreased inspired oxygen percentage, decreased ventilation or decreased transfer of oxygen across the alveoli, or ventilation/perfusion mismatch or right-to-left shunting of pulmonary blood flow. A decrease in haemoglobin concentration (anaemia) will occur due to blood loss or red cell destruction.

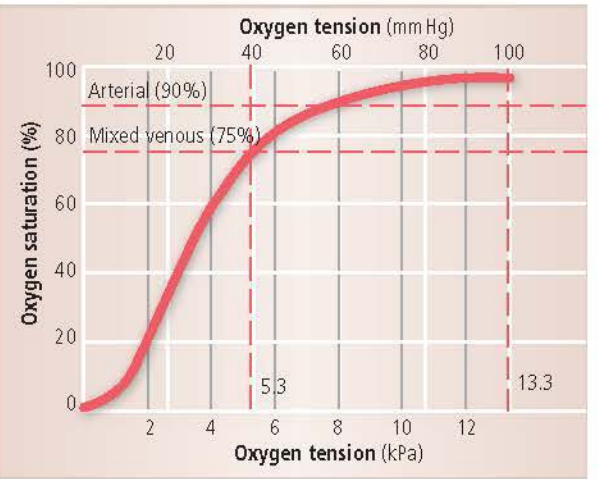
Hypoxaemia

Definition

Although only a small amount of oxygen is carried dissolved in blood, assessment of oxygenation is frequently performed by measurement of PaO_2. Severe hypoxaemia is defined as a PaO_2 of <60 mmHg (8 kPa). This is equivalent to an SpO_2 of 90% (**24**). SpO_2 is measured using pulse oximetry (see below). For animals with intracranial disease, it is recommended that the PaO_2 is maintained at >80 mmHg (10.7 kPa) to prevent increases in ICP.

Common causes of hypoxaemia in animals with neurological disease

- Aspiration pneumonia. Animals with CN deficits associated with brainstem or neuromuscular disease are predisposed to regurgitation and aspiration due to impairment of upper respiratory tract (URT) function. Recumbency and severe depression also predispose the animal to aspiration.
- Atelectasis (**25**). Recumbency, immobility and a high inspired oxygen concentration all predispose to alveolar collapse. This creates a mismatch in ventilation and perfusion and results in shunting of blood through the lungs. The shunt prevents oxygenation of the blood as it bypasses ventilated alveoli.
- Acute lung injury (ALI). Lung injury secondary to systemic inflammation, prolonged exposure to high inspired oxygen concentrations and trauma due to high ventilation pressures all contribute to the incidence and severity of ALI. These processes cause the release of inflammatory mediators within the lung, which stimulate a vicious cycle of pathological changes within the alveoli and surrounding lung tissues. The net result is interference with pulmonary gas exchange. ALI is tentatively diagnosed when the ratio of arterial oxygen tension



▲ **24** Oxygen–haemoglobin dissociation curve.



◀ **25** Recumbency and immobility are very common causes of atelectasis and hypoxaemia in the neurological patient.

▼ **26** Pneumothorax secondary to chest trauma, as shown in this lateral radiograph, can contribute to hypoxaemia in animals with concurrent head trauma. (Photo courtesy Shannon Holmes)



to fractional inspired oxygen concentration (PaO_2:FiO_2) is <300. Supportive care of ALI is based on supplemental oxygenation via mask, nasal catheters or oxygen cage.

- Acute respiratory distress syndrome (ARDS). ARDS occurs as the pathological changes in ALI progress and cause greater interference with gas exchange. ARDS is defined as a PaO_2:FiO_2 ratio of <200. These patients require ventilatory support.
- Pulmonary contusions or pneumothorax (**26**) in animals with concurrent chest trauma.
- Neurogenic or non-cardiogenic pulmonary oedema occurs in response to increased sympathetic nervous system stimulation and blood pressure (BP) secondary to brainstem ischaemia or compression. URT obstruction may also cause pulmonary oedema if the negative pressures generated during inspiration damage the alveolar membrane, causing fluid to flood the alveoli.
- Hypoventilation. In an animal breathing room air, hypoventilation causes increased alveolar CO_2, which dilutes alveolar oxygen and results in less oxygen being available to diffuse into the arterial blood. Restoring normal CO_2 values by the use of ventilation should also correct the hypoxaemia. If the hypoxaemia is not corrected with ventilation and the return of CO_2 to normal, then other causes of hypoxaemia need to be investigated.

Management

Hypoxaemia is managed by treating the underlying cause when possible and providing supplemental oxygen (see below) until the cause of the hypoxaemia has been corrected.

Anaemia

The clinical significance of anaemia varies according to whether the anaemia is acute or chronic:

- Acute anaemia (e.g. haemorrhage): clinical signs will usually occur if the PCV (packed cell volume) is <0.30 l/l (30%) in dogs and <0.25 l/l (25%) in cats.
- Chronic anaemia (e.g. haemolytic anaemia): clinical signs will generally be apparent when the PCV is <0.20 l/l (20%) in dogs and <0.15 l/l (15%) in cats.

Causes of anaemia in neurological disease

The most common cause is haemorrhage secondary to trauma or surgical blood loss.

Management

The definitive treatment for reduced tissue oxygenation due to anaemia is whole blood or red blood cell (RBC) transfusion. For further information on blood transfusion see Chapter 31.

If there is a delay in administering blood or RBCs, oxygen supplementation can be useful. While oxygen supplementation in these cases may only provide extremely small amounts of dissolved oxygen in the blood, this can be life saving in the short term.

Treatment methods for supplementing oxygen

Increasing the FiO_2

The aim of techniques that increase the inspired percentage of oxygen is to use the lowest FiO_2 that will maintain the PaO_2 at between 80 and 100 mmHg (10.7–13.3 kPa). As haemoglobin is fully saturated when the PaO_2 is approximately 100 mmHg (13.3 kPa), further increases in arterial oxygen tension produce very little increase in the amount of oxygen carried by the blood. In addition, there is an increased risk of lung damage as exposure to higher than normal levels of alveolar oxygen triggers pathological changes within the pulmonary tissues (oxygen toxicity). The higher the alveolar oxygen tension and the longer the duration of treatment, the greater the risk of irreversible alveolar damage.

Increased inspired oxygen can be delivered by a number of methods, including oxygen cage, head collar, mask or nasal catheter.

- **Oxygen cage.** Cages are useful for initial stabilization of small dogs and cats in respiratory distress while minimizing the stress of handling (**27**). The advantage of using an oxygen cage is that an FiO_2 of >50% can be achieved when the cage remains closed. The disadvantages include limited access to the patient if continuous oxygen support is required. In addition, patients are also at risk of hyperthermia and should be monitored carefully.
- **Head collar.** Head collars can be used for larger animals where size prevents the use of oxygen cages. The use of head collars covered with plastic film can provide a personalized oxygen cage. Oxygen is delivered via tubing attached on the inside of the head collar (**28**). Head collars have the advantage of providing a high FiO_2 while still allowing access to the rest of the animal. The disadvantages include:
  - The risk of jugular occlusion and increased ICP if the collar is too tight.
  - Hypercapnia can occur if the collar is tight, the oxygen flow is too low or the supply tubing becomes disconnected, allowing CO_2 to build up within the enclosed head collar. Hypoxaemia will also develop if the oxygen tubing detaches. Flow rates equivalent to those used in non-rebreathing anaesthetic systems (200–300 ml/kg/minute) are probably adequate.
  - Hyperthermia can also occur with this technique as the animal is rebreathing expired warm and humidified air.



▶ **27** **An oxygen cage can be used to provide oxygen supplementation in small- to medium-sized animals.**



▲ 28 A head collar covered in plastic film can be used to provide oxygen supplementation to larger animals when other methods are not feasible. Care should be taken to avoid jugular vein compression and overheating.



▲ 29 Face masks can be used to provide oxygen during initial stabilization or prior to induction of anaesthesia.



▲ 30 'Flow-by' oxygen therapy can be used to provide short-term oxygen supplementation to animals that will not tolerate a face mask.



▲ 31 Nasal catheters can be used to provide continuous oxygen supplementation and also allow continuous access. They should be avoided in animals with increased intracranial pressure, coagulopathy and nasal fractures.

- **Face mask.** Face masks are generally used for initial stabilization only, particularly in animals not amenable to oxygen cages due to their size (**29**). The advantage of using face masks for oxygen supplementation is that they are easily accessible and allow for prompt administration of oxygen in an emergency setting. One of the disadvantages is that animals in respiratory distress may not tolerate a mask held over their face. In these cases 'flow-by' oxygenation can be used (**30**). A tight-fitting mask can also exacerbate hyperthermia, as rebreathing of expired humidified gases occurs. An open mask or flow-by technique provides limited increase in FiO_2.
- **Nasal catheter.** An intranasal catheter is inserted into the ventral nasal meatus, directing the catheter ventromedially (**31**). The tip can be positioned just inside the nostril or in the nasopharynx.

To position the catheter tip in the nasopharynx, the catheter should be pre-measured to the level of the medial canthus to ensure correct positioning. If the tip is inserted too far, it risks being introduced into the oesophagus, causing aerophagia and gastric dilation. Most animals will tolerate an oxygen flow of 100 ml/kg/minute/nostril. Higher flows may cause increased irritation, sneezing or removal of the catheter by the patient. If flows >100 ml/kg/minute are required to achieve adequate oxygenation, a catheter can be placed in each nostril, allowing a total oxygen flow of up to 200 ml/kg/minute to be delivered comfortably. Nasal catheters have the advantage of allowing long-term supplementation of oxygen in animals with respiratory disease and continuous access to the patient. Furthermore, there is no risk of hyperthermia or hypercapnia. The disadvantages include sneezing associated with placement of nasal catheters, which can be detrimental if there is: (1) increased ICP, as sneezing will cause further increases, which may result in fatal herniation of the brainstem, or (2) coagulopathy, as sneezing may cause bleeding from the nostril or haemorrhage into the eye or brain. This procedure should also be avoided in the head-trauma patient, when fractures within the nasal cavity can lead to misplacement of the catheter within neural tissue. Finally, there is a limited increase in FiO_2 of 0.3–0.4 (30–40% inspired oxygen concentration) observed with this method.



▲ **32** **Endotracheal intubation and delivery of high inspired oxygen concentration may be needed in animals that do not improve with other methods of oxygen supplementation.**



▲ **33** **Mechanical ventilation is commonly used to 'breathe' for patients that have inadequate spontaneous ventilation or are unresponsive to other methods of oxygen supplementation.**

Endotracheal intubation

Endotracheal intubation and connection to a breathing system may be necessary when other methods of increasing FiO_2 fail to achieve adequate arterial oxygen tension or if the animal becomes increasingly depressed (**32**). Intubation must be performed before the animal becomes unconscious. This will require careful administration of intravenous anaesthetic agents. If intubation is delayed until the animal becomes unconscious because of the pathological process, cardiopulmonary arrest is highly likely.

Endotracheal intubation has the advantage of allowing connection to a breathing system and the delivery of 100% oxygen. The clinician can therefore be more confident of the delivered FiO_2. Disadvantages include: (1) maintenance of oral endotracheal tubes generally requires some degree of sedation or anaesthesia and (2) the depressant effects of sedative and anaesthetic agents will also necessitate some form of positive pressure ventilation, particularly in animals with intracranial disease where maintenance of normal $PaCO_2$ is essential.

Assisted ventilation is indicated when increasing FiO_2 fails to correct hypoxaemia (**33**). Details of ventilation techniques are described in the next section.

VENTILATION

The aim of mechanical ventilation is to recruit and stabilize alveoli and deliver oxygen to and remove carbon dioxide from them without causing lung injury. Careful monitoring of ventilation to ensure normocapnia and satisfactory oxygenation is essential to guide management strategies. Furthermore, the haemodynamic consequences of mechanical ventilation should be continuously monitored. During spontaneous ventilation, a negative pressure is created within the thoracic cavity to draw air into the lungs. During mechanical ventilation, a positive pressure is generated to push gas into the lungs. This positive pressure compresses blood vessels within the chest, especially in the low-pressure venous circulation and right side of the heart. The net effect is a decrease in cardiac output. Ideally, cardiac output should be monitored in ventilated animals, but arterial BP measurement is a common surrogate measure in a clinical setting.

Mechanical ventilation is indicated in animals with respiratory failure. Respiratory failure can be divided into two types:

- **Hypercapnic ventilatory failure** (inadequate alveolar ventilation = hypoventilation): generally considered to be present when the $PaCO_2$ is >50 mmHg (6.7 kPa). Ventilatory failure should also be considered in animals with normal $PaCO_2$ if there is: (1) clinical evidence of increased respiratory work and impending fatigue (high respiratory rate; change in respiratory pattern; increased inspiratory effort; erratic changes in tidal volume and/or respiratory frequency), or (2) inadequate respiratory compensation for metabolic acidosis. In animals with intracranial disease, any increase in CO_2 may have detrimental effects on ICP. Mechanical ventilation is required in any animal with intracranial disease if the $PaCO_2$ is >40 mmHg (5.3 kPa). The causes of ventilatory failure in animals with neurological disease include:
  - Neuromuscular weakness: tetrodotoxin, snake envenomation, tick paralysis, botulism, polyradiculoneuritis, myasthenia gravis (MG).
  - Cervical spinal cord injury.
  - Intracranial disease with involvement of respiratory centres (i.e. caudal fossa pathology).
  - Drug-induced CNS depression: anaesthesia, opioid overdose.
- **Hypoxaemic respiratory failure** (inadequate oxygen exchange): generally defined as arterial oxygen tension <60 mmHg (8 kPa) when the FiO_2 is >0.5.

Treatment methods for providing ventilation

The most common type of ventilation used routinely in animals is intermittent positive pressure ventilation (IPPV). The factor determining the termination of inspiration and the onset of expiration is most often volume, pressure or time. Positive end-expiratory pressure (PEEP) and continuous positive airway pressure (CPAP) are also used, particularly in animals with pulmonary pathology. *Table 6* gives a summary of the modes of ventilation that can be used in neurological patients.

Table 6 **Modes of mechanical ventilation**

MODE	MECHANISM	USES/ADVANTAGES	DISADVANTAGES/CAUTIONS
Volume-cycled IPPV	Inspiration terminated when pre-set volume delivered. Delivers desired V_T regardless of lung compliance	Preferred use in normal lungs	Increases risk of lung injury in animals with altered lung compliance
Pressure-cycled IPPV	Inspiration is terminated when a pre-set pressure is delivered. V_T will therefore be determined by lung and chest wall compliance	Preferred method for animals with altered lung compliance or very small patients	Poor airway, lung or chest wall compliance will require high inflation pressures to achieve an adequate minute volume

(Continued)

Table 6 **Modes of mechanical ventilation** (*continued*)

MODE	MECHANISM	USES/ADVANTAGES	DISADVANTAGES/CAUTIONS
Time-cycled IPPV	Inspiration is terminated when a set inspiration time has passed. V_T is determined by lung and chest wall compliance	Infrequently used in current clinical practice	PIP is determined by lung and chest wall compliance. Decreases in compliance will cause increases in PIP and increase risk of injury
OTHER DEFINITIONS			
PEEP	Maintains positive pressure at the end of expiration during controlled ventilation, preventing complete alveolar collapse at the part of the respiratory cycle when airway pressure is usually 0 cmH_2O	Minimizes atelectasis and associated ventilation/perfusion mismatch in normal lungs. Minimizes volutrauma in lung pathology	High PEEP may compromise venous return and cardiac output. Decreased venous return can lead to increased cerebral blood volume and increased ICP
CPAP	Technique used in spontaneously breathing animals to prevent alveolar collapse at the end of expiration and increase functional residual capacity	Can help stabilize open alveoli and prevent alveolar collapse. May improve oxygenation in spontaneously breathing animals and negate need for IPPV	Animals may not tolerate nasal catheters or prongs. Higher than normal pressure at the end of expiration may compromise venous return and cardiac output

V_T = tidal volume; PEEP = positive end-expiratory pressure; CPAP = continuous positive airway pressure; ICP = intracranial pressure; PIP = peak inspiratory pressure; IPPV = intermittent positive pressure ventilation.

A wide range of other ventilation strategies are used to promote ventilation and oxygenation, minimize lung injury and prevent haemodynamic compromise. Techniques including high-frequency ventilation, inverse ratio ventilation, biphasic airway pressure and extracorporeal membrane oxygenation have been used to reduce airway pressures in human patients with severe pulmonary disease. These techniques are limited to specialist centres with specialist equipment, a thorough understanding of which is essential before embarking on either short- or long-term management. A detailed description of the equipment and techniques is beyond the scope of this book. For more information, the reader is referred to the Further reading list, p. 623.

Adverse effects of ventilation

Mechanical ventilation may have numerous adverse effects on a variety of body systems, including the cardiovascular, respiratory, neurological, renal and gastrointestinal systems. A summary of these effects and how to minimize them is given in *Table 7*. Before ventilation of any animal is undertaken it is essential to understand the potential adverse effects and how to avoid them.

Guidelines for use of mechanical ventilation

The aim of ventilation is to optimize oxygenation and ventilation, while minimizing adverse effects on cardiovascular, pulmonary and neurological functions.

Different ventilatory strategies are used to manage different types of respiratory failure. The ventilation strategy may need to be further altered if the animal has concurrent intracranial disease. Guidelines for use of ventilation in these situations are described below (see also *Table 8*, page 46).

Table 7 **Adverse effects of mechanical ventilation**

SYSTEM	EFFECT	METHODS OF MINIMIZING ADVERSE EFFECTS
Cardiovascular	Positive airway pressure during IPPV interferes with venous return and CO during inspiration. CPAP and PEEP interfere with venous return and CO during expiration. PEEP in combination with IPPV interferes with venous return throughout the respiratory cycle. Decreased CO leads to decreased oxygen delivery to the tissues and may offset improvement in oxygen content	• To minimize the detrimental effects on cardiovascular performance it is important to ensure adequate blood volume and minimize PIP, the amount of time spent in inspiration (inspiratory time) and PEEP. • Monitor blood pressure and CVP during ventilation. • Monitor ICP in animals with intracranial disease.
Pulmonary	Barotrauma: excessive airway pressure causes physical disruption of lung tissue and extra-alveolar air (e.g. pneumothorax). Volutrauma: overdistension of alveoli causes increased permeability, oedema and inflammation. Repetitive stretching and recoil of alveoli induces inflammatory and structural changes, leading to increased permeability of alveoli and oedema formation. Inflammation associated with ventilator-induced lung injury may be an important inciting factor for development of SIRS and MOF	• Use the minimum V_T and PIP necessary to achieve adequate oxygenation and ventilation. • Lung disease: lower V_T, higher RR and PEEP. Slight hypoventilation and permissive hypercapnia ($PaCO_2$ 45–60 mmHg). *Note:* Permissive hypercapnia must be avoided in patients with intracranial disease.
Renal function	Decreased urine output due to release of ADH and decreasing ANP production causing fluid retention. Decreased GFR and intrarenal blood flow redistribution may interfere with the renal elimination of drugs	• Use the minimum V_T and PIP necessary to achieve adequate oxygenation and ventilation.
Gastrointestinal system	Increased incidence of gastric ulceration and liver dysfunction. Decreased portal blood flow may also reduce the elimination of drugs that undergo hepatic metabolism	• Use the minimum V_T and PIP necessary to achieve adequate oxygenation and ventilation.
Central nervous system	Interference with venous return can lead to increased cerebral venous blood volume and ICP	• Use the minimum V_T and PIP necessary to achieve adequate oxygenation and ventilation. • Neuromuscular relaxation in anaesthetized animals can help reduce the PIP required to ventilate to normocapnia. • Use PEEP very carefully in animals with intracranial disease. • Monitor CVP and ICP in animals with intracranial disease.

V_T = tidal volume; RR = respiratory rate; PIP = peak inspiratory pressure; PEEP = positive end-expiratory pressure; CPAP = continuous positive airway pressure; ICP = intracranial pressure; CVP = central venous pressure; CO = cardiac output; GFR = glomerular filtration rate; SIRS = systemic inflammatory response syndrome; MOF = multiple organ failure; ADH = antidiuretic hormone; ANP = atrial natriuretic peptide; IPPV = intermittent positive pressure ventilation.

Table 8 **Guidelines for mechanical ventilation**

	NORMAL LUNGS	ABNORMAL LUNGS	INTRACRANIAL DISEASE
Preferred ventilator type	Pressure or volume cycled	Pressure cycled	Pressure cycled
Settings			
V_T	10–20 ml/kg	<6 ml/kg	Settings are a compromise between pre-existing lung condition and need to maintain normocapnia and prevent increased ICP
RR	Comparable to resting respiratory rate	Adequate to maintain appropriate $F'ETCO_2$	
I:E ratio	1:3	1:3	
PIP	10–20 cmH_2O will adequately ventilate most animals with normal lungs; cats will sometimes require <10 cmH_2O due to higher chest compliance	Higher PIP required due to reduced compliance (see Further reading)	Use the minimal PIP required to achieve normoxia and normocapnia, but limit adverse effects on venous drainage and ICP
PEEP	0–5 cmH_2O	Start at 3 cmH_2O and increase up to 10 cmH_2O as required to achieve adequate oxygenation without decreasing oxygen delivery	Avoid/use carefully in animals with intracranial hypertension

V_T = tidal volume; RR = respiratory rate; I:E ratio = inspiratory:expiratory time ratio; PIP = peak inspiratory pressure; PEEP = positive end-expiratory pressure; ICP = intracranial pressure; $F'ECO_2$. = Fractional concentration of carbon dioxide in mixed expired air

Mechanical ventilation in cases of ventilatory failure

In animals with ventilatory failure, peak inspiratory pressure (PIP) is adjusted until the minimum pressure that maintains adequate ventilation and oxygenation is obtained. For normal chests, a PIP of 8–10 cmH_2O in dogs and slightly less in cats will adequately ventilate most animals in normal body condition. Higher pressures may be required in obese animals and animals with barrel chests.

The majority of these animals will have normal lungs at least initially, so only conservative PEEP may be required (up to 3 cmH_2O). This will help prevent the development and progression of atelectasis, especially if a high FiO_2 is used. PEEP must be used with extreme care in animals with increased ICP.

Mechanical ventilation of animals with lung pathology in the absence of intracranial disease

Smaller tidal volumes (5–6 ml/kg) and higher respiratory rates are recommended in animals with diseased lungs to prevent overdistension of normal lung tissue. Overdistension of normal lungs occurs as gas delivered during the inspiratory phase follows the pathway of least resistance and distributes to areas of lung that are more compliant (i.e. normal lung tissue is preferentially ventilated compared with less compliant diseased tissue). Overdistension of normal lung contributes to ventilator-induced lung injury (VILI) and triggers a cascade of worsening pulmonary function and the development of multiple organ failure. Unfortunately, this type of ventilation strategy is unable to maintain normal CO_2. However, in animals with normal intracranial compliance the increases in PaO_2 are generally tolerated.

PEEP is particularly useful in animals with reduced lung compliance, as there is a tendency for lungs to collapse during expiration. In these conditions, PEEP prevents alveolar collapse and atelectasis. By preventing alveolar collapse, PEEP prevents the cyclic collapse and re-opening of alveoli that contribute to VILI. By minimizing atelectasis, PEEP also reduces physiological dead space and improves pulmonary gas exchange.

Adverse effects of PEEP includes interference with normal venous return during the expiratory phase of ventilation. To minimize this effect, the amount of PEEP

applied is adjusted to optimize arterial oxygenation while maintaining normal cardiac output (and oxygen delivery). Clinically, where measurement of cardiac output is not available, the effect of IPPV on arterial BP and central venous pressure (CVP) can be used to assess the impact on cardiovascular function.

Mechanical ventilation of animals with lung pathology in the presence of intracranial disease

Ventilation of animals with both lung and intracranial disease presents a unique challenge, as many of the ventilator strategies designed to minimize VILI have a detrimental effect on ICP.

The low tidal volume ventilation strategies recommended in animals with lung pathology cause permissive hypercapnia and are harmful in animals with intracranial disease, as a marked increase in ICP accompanies increasing $PaCO_2$. Increasing mean airway pressure also has the potential to increase ICP due to detrimental effects on venous return increasing cerebral blood volume. The level of PIP required to ventilate these animals adequately may be reduced by use of non-depolarizing neuromuscular blockers, which increase compliance of the chest wall. Venous return is optimized by increasing expiratory time and, thus, the time for blood to return to the heart. PEEP should be avoided or used extremely carefully in animals with intracranial disease. (For details of neuromuscular blockers see Chapter 29.)

Increases in ICP negate any improvement in oxygenation by reducing cerebral perfusion pressure (CPP). Furthermore, increased ICP increases the risk of herniation and death. The use of ICP monitoring may be worthwhile in animals with concurrent intracranial disease and lung disease warranting mechanical ventilation to ensure ventilation strategies do not exacerbate intracranial hypertension. (For more details on ventilation in ARDS see Further reading.)

Ventilation of animals with pulmonary disease and concurrent CNS disease requires intensive monitoring of pulmonary, cardiovascular and neurological functions. This is limited to referral hospitals.

CARE OF THE VENTILATED ANIMAL

Appropriate monitoring and supportive care of the ventilated patient are required to minimize adverse effects of chronic intubation, ventilation and recumbency. This section discusses some important aspects of this care. *Table 9* gives a summary of the general nursing requirements of these animals.

Table 9 **General nursing of the ventilated patient**

PROCEDURE	RATIONALE
Lubricate eyes	Paralysed animals are unable to close eyelids and are predisposed to corneal ulcers if eyes are allowed to dry out
Moisten and reposition tongue every 1–2 hours	Prevents desiccation, circulatory stasis and swelling. Wrapping the tongue in a swab soaked with water can be useful for preventing desiccation
Reposition endotracheal tube every 2 hours	Prevents local tracheal necrosis at site of inflated cuff. Do not inflate the cuff of the ETT excessively. The cuff should be inflated until there is no audible leak during inspiration. High-volume low-pressure cuffs are preferred. Ties used to secure the ETT in place should also be repositioned every 2–4 hours to prevent circulatory stasis of muzzle
Swab pharynx and suction stomach/ oesophagus every 2 hours	Helps minimize regurgitation and aspiration. Even when the cuff of the ETT is inflated, fluid can accumulate proximal to the cuff and enter the airway when the cuff is deflated. It is important that animals with intracranial disease are adequately sedated or anaesthetized during this procedure, as coughing will cause a marked increased in ICP

(Continued)

Table 9 **General nursing of the ventilated patient** (*continued*)

PROCEDURE	RATIONALE
Positioning	Maintain in sternal recumbency if possible, as this optimizes pulmonary and cardiovascular functions. If positioned in lateral recumbency, turning every 2 hours may help prevent atelectasis and compression of dependent muscle groups
Head elevation	In animals with intracranial disease the head should be supported so that it is level with or slightly above the heart in order to encourage venous drainage. Excessive elevation of the head will impair perfusion. Care must be taken to avoid jugular venous occlusion
Environmental temperature control	Monitor body temperature and warm as needed using circulating warm air, blankets, heating pads or hot water bottles. Care must be taken to avoid discomfort or burns from the heat source
Clean and dry	Incontinence pads can be used, but must be changed regularly; alternatively, place an indwelling urinary catheter

Sedation/analgesia

Most animals with respiratory disease will require anaesthesia to allow endotracheal intubation and ventilation. Some degree of sedation or anaesthesia will also be required in animals with neuromuscular disease, particularly during recovery when animals will attempt to move, but are still too weak to maintain their own spontaneous ventilation or protect their upper airway. If anaesthesia is not required to maintain immobility (e.g. animal paralysed by snake envenomation), it is important to remember that these animals are conscious and aware of environmental stimuli, including noise and touch. Some form of analgesia/sedation is recommended to minimize the stress associated with handling. Agents used to sedate/anaesthetize animals requiring ventilation are discussed in Chapter 29.

Monitoring

As mechanical ventilation may have detrimental effects on a variety of organ systems, close monitoring of ventilated animals is essential.

Cardiovascular function

To ensure adequate circulating blood volume and BP and to minimize the detrimental effects of ventilation on cardiovascular function, measurement of arterial BP and CVP should be performed in ventilated animals. These techniques are described in detail in Monitoring the cardiovascular system, p. 56.

Pulmonary function

Adequacy of ventilation

Assessment of the adequacy of ventilation can be made by measurement of airway pressure, capnography (see p. 50) and measurement of arterial CO_2.

Measurement of airway pressure is essential whenever mechanical ventilation is performed, as sudden changes in pressure can have dramatic consequences. Failure to achieve a predetermined airway pressure indicates inadequate delivery of volume to the patient and may be due to insufficient gas supply, leaks in the breathing system or disconnection. Abrupt increases in airway pressure suggest sudden changes in compliance or resistance and can be caused by obstruction or kinking of tubing, acute bronchoconstriction or development of pneumothorax. Gradual increases in airway pressure suggest deterioration in pulmonary function, with associated decreases in compliance and increases in resistance.



▲ **34** **Multivariable monitoring recording haemoglobin saturation and plethysmograph using pulse oximetry. The level of CO_2 expired over time is measured using capnography (blue wave form). Arrow = end-tidal CO_2.**

Adequacy of oxygenation

The amount of oxygen within the blood can be assessed by measuring oxyhaemoglobin saturation (SpO_2) with a pulse oximeter (**34**) and measuring the partial pressure of oxygen in arterial blood (PaO_2). Calculation of oxygen delivery to the tissues requires measurement of both arterial oxygen content and cardiac output. Measurement of mixed venous oxygen can provide an indirect measure of adequacy of oxygen supply to the tissues. Details of these techniques are described below.



▲ **35** **A closed urinary collection system allows continuous monitoring of urine output in critical patients.**

Neurological function

Neurological function is influenced by the adequacy of oxygenation, ventilation and perfusion, and a reduction in these variables can lead to neurological deterioration. Deterioration of neurological status will be observed clinically by progressive mental depression in conscious animals, dilation of pupils with absence of a PLR and development of cardiorespiratory abnormalities (e.g. cardiac arrhythmias, Cushing reflex [reflex bradycardia], abnormal breathing patterns). ICP monitoring may also be useful in animals with concurrent intracranial and pulmonary disease, particularly in those requiring ventilation.

Renal function

Measurement of urine output (see p. 60) and urine specific gravity (SG) should be performed regularly in chronically ventilated animals to monitor the effects of ventilation on renal function and to assess fluid balance. Ideally, this should be performed via a sterile indwelling urinary catheter and closed collection system (**35**). Measurement of blood urea, creatinine and electrolytes should also be performed daily to monitor for changes in renal function.

Fluid therapy *(for more details see Chapter 31)*

Once volume deficits have been corrected, crystalloid fluids are required to maintain adequate hydration. As large amounts of water can be lost through evaporation from the airways of ventilated animals, particularly when non-rebreathing systems are used, it is generally recommended that fluid administration is supplied at 1.5–2 × maintenance to prevent dehydration and maintain adequate hydration of the airway mucosa. Humidification of ventilator gases will offset this effect.

In ventilated animals with intracranial disease, fluid therapy should ideally be monitored using CVP to prevent excessive fluid administration and increases in hydrostatic pressure.

Humidification of the airway

Ventilation with dry gases causes drying of airway secretions, decreased mucociliary clearance and associated increased risk of secondary infection. Water lost from the airway will increase fluid requirements. Adequate intravenous fluid therapy is essential for maintaining airway hydration, but heat and moisture exchange (HME) devices (see Chapter 29) placed between the animal and the breathing circuit can reduce water loss by up to 80%. These devices need to be replaced every 6 hours to ensure optimal efficiency.

Ideally, humidified gases should be used if ventilation is expected to be prolonged. Even a couple of hours of ventilation with dry gases can cause significant damage to the upper airways and lungs. Humidifiers can be fitted to most ventilators and are placed in the inspiratory limb of the ventilator breathing system. Sterile saline can be instilled into the airway at the level of the tracheal bifurcation and then removed via suctioning every 1–2 hours. As this increases the risk of nosocomial infection, suctioning is only recommended when secretions are excessive. Suctioning generally requires the patient to be disconnected from the ventilator (open suctioning). This predisposes to alveolar collapse. The performance of an alveolar recruitment manoeuvre may be necessary to re-recruit collapsed alveoli. Alveolar recruitment is achieved by manually inflating the lung with a larger than normal tidal volume or PIP than that being used for ventilation, holding for a prolonged inspiratory time.

Cardiovascular support in the ventilated patient

Vasoactive agents may be indicated in animals with hypotension unresponsive to normalization of blood volume and techniques used to reduce mean airway pressure during ventilation. Conservative approaches to the correction of hypotension should be performed first (fluid therapy and minimizing the delivery of vasodilating agents such as anaesthetics) and preparations made for the administration of vasoactive drugs if indicated. Close monitoring must be performed before, during and after pharmacological management of BP abnormalities. Pharmacological manipulation of BP is described in the sections on hypotension (p. 52) and hypertension (p. 55).

Monitoring oxygenation and ventilation

Pulse oximetry

The factors that interfere with a reliable pulse oximeter reading include local vasoconstriction, interference from extraneous lighting, movement, haemoglobin abnormalities and pigment. Pulse oximetry can be used to provide a guide to oxygenation. It provides a non-invasive beat-by-beat assessment of the amount of oxygen carried by haemoglobin within the arterial blood. However, to ensure accuracy, the pulse quality must be good and reflected in the generation of a continuous plethysmogram.

Pulse oximetry measures the percentage of haemoglobin (Hb) molecules that are saturated with oxygen and the pulse rate. Due to the shape of the oxyhaemoglobin dissociation curve (see **24**), a saturation of >95% is required to ensure a PaO_2 of >80 mmHg (10.7 kPa). There are many physiological and technical factors that can interfere with the pulse oximeter, so the readings should be interpreted with a thorough understanding of the limitations of the equipment. (*Note:* Pulse oximetry does not assess the adequacy of ventiliation and severe hypercapnia can develop despite adequate oxygen saturation, especially if the patient is inspiring gases with a high FiO_2. Pulse oximetry can only be relied on to measure oxyhaemoglobin saturation and pulse rate.)

Capnography

Capnography provides a breath-by-breath assessment of the adequacy of ventilation, assuming normal cardiovascular function. This technique measures CO_2 in the expired patient gases ($P'ETCO_2$) (see **34**), which approximates the CO_2 tension in the alveoli ($PACO_2$). As alveolar gases should be in equilibrium with arterial blood, $P'ETCO_2$ can be used to approximate $PaCO_2$.

Intermittent analysis of arterial blood gas samples should also be performed to ensure capnography is providing a reliable indication of ventilation, as discrepancies between arterial and end-tidal CO_2 can occur. Differences between $PaCO_2$ and $P'ETCO_2$ are caused by reduced pulmonary blood flow (and increased physiological dead space) due to pulmonary thromboembolism, air embolism and reduced cardiac output (heart failure, hypovolaemia). In small animal patients



▲ 36 A humidifying and moisture exchange (HME) device, placed between the patient and the anaesthetic circuit, prevents excessive heat and fluid loss during anaesthesia. A capnograph attached to the HME provides breath-by-breath assessment of adequacy of ventilation.

with cardiovascular compromise, $PaCO_2$ may differ from $P'ETCO_2$ by 10–20 mmHg or more due to development of physiological dead space. Discrepancies will also occur due to increased dead-space ventilation, as less of the inspired tidal volume actually reaches the alveoli. An example of this is panting in a spontaneously breathing animal.

As capnography provides breath-by-breath information and is a non-invasive monitor, it is an important tool for assessing pulmonary and circulatory emergencies in the ventilated patient (**36**).

Arterial blood gases

Measurement of PaO_2 is the gold standard for determining the amount of oxygen within arterial blood and should be performed whenever the accuracy of pulse oximetry is in doubt. Measurement of mixed venous oxygen tension (blood collected from the right atrium via a central venous catheter) can provide an indication of the relationship between oxygen supply and demand. An increase in the difference between arterial and mixed venous oxygen tension suggests either decreased tissue perfusion or increased tissue consumption.

Calculation of oxygen delivery

Oxygen delivery to tissues is a product of cardiac output and arterial oxygen content ($DO_2 = CO \times CaO_2$). A calculation of DO_2 is the ultimate measure of adequacy of tissue oxygenation, but is not always practical. CaO_2 is easily calculated, as it is the sum of oxygen bound to haemoglobin and oxygen dissolved in the plasma ($CaO_2 = [SpO_2 \times Hb \times 1.34] + [0.003 \times PaO_2]$). Because of the requirement for specialist equipment, assessment of cardiac output is usually limited to referral institutions. As a result, cardiac output is usually extrapolated from the measurement of BP (mean arterial pressure [MAP] = cardiac output × systemic vascular resistance [SVR]). An inability to obtain direct measurement of cardiac output prevents the calculation of DO_2 in a clinical setting.

CIRCULATION: CARDIOVASCULAR SUPPORT OF THE NEUROLOGICAL PATIENT

Abnormalities of cardiovascular function can cause secondary neurological damage in animals with intracranial disease. Hypotension leads to reduced CPP, particularly in the presence of increased ICP (CPP = MAP – ICP). Hypertension has the potential to increase ICP in the presence of intracranial disease. This occurs when increases in MAP are in excess of normal autoregulation or when autoregulation is impaired. When autoregulation is impaired, any increase in MAP can cause linear increases in cerebral blood volume and ICP. Therefore, cardiovascular function needs to be monitored closely in neurological patients and hypotension and hypertension managed as required.

Circulatory shock/hypotension

Definition

Circulatory shock causes a significant reduction in organ perfusion. During the compensatory phase, BP is maintained by the responses to reduced tissue perfusion, including increases in heart rate (**37, 38**), peripheral vasoconstriction, shifts in fluid from the interstitial space to the intravascular space and reduced urine production. Once the fluid deficit exceeds the ability of the body to compensate (decompensatory shock), decreases in BP occur (**39**).

In humans with head trauma, hypotension is defined as systolic arterial blood pressure (SAP) ≤90 mmHg. Similar limits of MAP in the trauma patient have not been established in small animals, although maintenance of CPP (MAP – ICP) at between 60 and 70 mmHg and MAP >70 mmHg is associated with a better outcome in head-trauma cases. In the absence of ICP monitoring it is recommended that the MAP should be 70–80 mmHg and the SAP should be 100 mmHg to maintain CPP in the presence of increased ICP. Further increases in CPP above 70 mmHg are not recommended, as the use of aggressive fluid therapy and vasopressors to maintain CPP above 70 mmHg is associated with systemic complications such as ARDS.

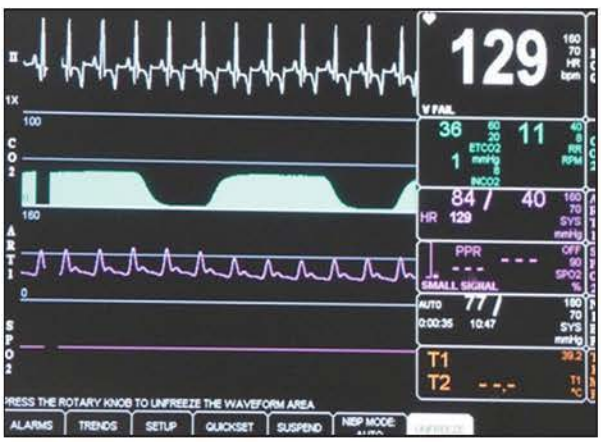
Clinical signs of circulatory shock

Instigation of appropriate therapy is dependent on early recognition of shock. This requires a good understanding of the clinical signs of circulatory shock. The clinical signs of shock will vary depending on the severity, the degree of compensation and the cause.

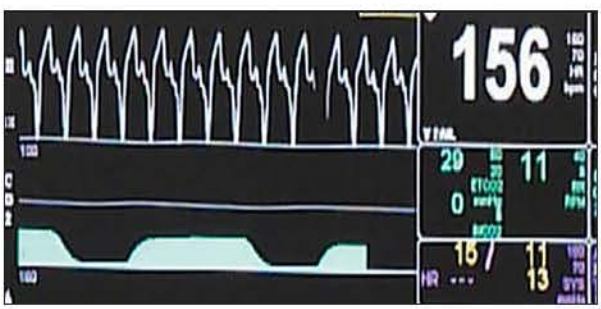
Reduction in cardiac output causes sympathetic nervous stimulation, leading to tachycardia and peripheral vasoconstriction (pale mucosal membranes, cold extremities, reduced rectal temperature). If these changes can compensate for the reduction in cardiac output, BP will be normal. Once these compensatory responses are overwhelmed, BP will decrease. It is essential that therapy is started before decompensation and decreases in BP occur in order to minimize organ damage.



▲ **37** Recording from a patient taken before blood loss. Heart rate (seen here to be **106** beats per minute) and blood pressure (wave marked with arrow), measured using an arterial catheter, are within normal ranges.



▲ **38** When loss of blood volume is severe or prolonged, compensatory mechanisms fail and hypotension occurs, as can be seen in this recording.



▶ **39** Electrocardiogram showing tachyarrhythmia, here associated with poor cardiac output and hypotension. In this case urgent management is required, including rapid correction of the cause of the arrhythmia.

Management of circulatory shock

Appropriate treatment depends on the cause. Arterial BP is influenced by cardiac output and total peripheral resistance. A decrease in either cardiac oputput or total peripheral resistance will decrease BP. Cardiac output is the product of heart rate and stroke volume. Stroke volume is determined by preload (blood volume), myocardial contractility and afterload.

Hypovolaemic shock

A reduction in circulating blood volume results in a decreased amount of blood returning to the heart (preload), with a resultant decrease in stroke volume and cardiac output and, therefore, BP. The most common cause of hypovolaemic shock in the neurological patient is haemorrhage associated with trauma or surgical losses. Trauma may also cause hypovolaemia due to loss of protein-rich fluid into damaged tissues such as muscle bruises and large wounds. In immobile animals unable to access water, dehydration may lead to hypovolaemia once the fluid deficit exceeds 10% of body weight.

Fluid therapy forms the cornerstone of the management of hypovolaemia. (For details on fluid therapy see Chapter 31.)

Vasodilatory/distributive shock

Vasodilatory shock is caused by marked peripheral vasodilation, which results in relative hypovolaemia as the vascular volume increases relative to the volume of blood within the circulation. A primary cause of peripheral vasodilation and hypotension in animals with neurological disease is spinal disease that interferes with the sympathetic innervation of the splanchnic vasculature. A secondary cause is the use of anaesthetic agents that cause peripheral vasodilation (e.g. propofol, isoflurane, sevoflurane). Vasodilation associated with administration of these agents is dependent on the dose and rate of administration. The higher the dose or the faster the rate of administration, the greater the amount of vasodilation and the lower the BP. Vasodilation and hypotension will also occur in any animal that develops concurrent systemic inflammatory response syndrome (SIRS). SIRS may develop in the presence of any factor that can stimulate a widespread inflammatory response (e.g. multiple organ trauma, hypoxaemia and ventilator-induced lung injury).

In most cases, management requires treatment of the underlying cause. Symptomatic treatment includes fluid therapy and administration of vasoconstrictive agents. Drugs used to increase BP in human patients with head trauma include noradrenalin (norepinephrine) infusion, dopamine and phenylephrine. Vasopressin has also been used to increase BP in critically ill animals with SIRS. The dose rates of those agents that have been used in small animals are: noradrenalin (norepinephrine) (0.05–2 µg/kg/minute); dopamine (5–10 µg/kg/minute); vasopressin (0.5–2 IU/kg/minute) and phenylephrine (1–3 µg/kg/minute) (see Further reading).

When sedative and anaesthetic agents are responsible for the hypotension, the dose of the administered agent should be reduced and fluid therapy given to animals that do not respond to the reduction in anaesthesia.

Cardiogenic shock

Cardiogenic shock may occur due to marked changes in heart rate and rhythm, and reduced myocardial contractility. Abnormalities in cardiac rhythm include those associated with fast heart rates (tachyarrhythmias) and slow heart rates (bradyarrhythmias). Hypotension occurs secondary to fast heart rates, as there is decreased time for the heart to fill during diastole, resulting in reduced stroke volume and cardiac output. In addition, the high heart rate increases myocardial oxygen demand when oxygen delivery may be compromised. This predisposes to myocardial ischaemia, which may further exacerbate the arrhythmia. Slow heart rates cause hypotension, as cardiac output is dependent on heart rate ($CO = SV \times HR$). Poor myocardial contractility decreases the amount of blood able to be pumped by the heart and, therefore, cardiac output.

Abnormalities in cardiac rhythm

Tachyarrhythmias

Causes of tachyarrhythmias associated with neurological disease include brainstem disease/compression. Myocardial degeneration and necrosis are also reported to occur following cranial and spinal trauma in dogs. Causes associated with other systemic abnormalities include myocardial contusions secondary to thoracic trauma and myocardial ischaemia secondary to hypovolaemia (e.g. haemorrhage from trauma or surgery). Fluid, electrolyte and acid–base abnormalities may also occur secondary to inappetence, an inability to eat and drink or losses from the gastrointestinal tract or kidneys. (For more details on fluid and electrolyte abnormalities that occur commonly in neurological disease see Chapters 3 and 31.) Persistent tachycardia can also lead to myocardial ischaemia and arrhythmias, as the increase in heart rate causes both an increase in myocardial oxygen consumption and a reduction in oxygen delivery due to decreased time for the heart muscle to be perfused.

Management of arrhythmias involves the correction of all possible underlying causes. Brainstem compression and/or herniation requires specific treatment for increased ICP (see Chapter 20). Brainstem ischaemia can occur due to either increased ICP or decreased BP. Any concurrent electrolyte and acid–base abnormalities also need to be corrected. Any cause of persistent tachycardia, including pain, hypovolaemia or hypotension, needs to be corrected to minimize the risk of exacerbating or contributing to the development of tachyarrhythmias.

Specific anti-arrhythmic medication is indicated if the arrhythmia persists despite treatment of all possible causes and/or if tissue perfusion is compromised. Specific anti-arrhythmics for ventricular tachyarrhythmias include lidocaine (sodium channel blocker) and beta blockers (e.g. esmolol). Supraventricular tachyarrhythmias can be treated using beta blockers. (For dose rates commonly used in clinical cases see Further reading.)

Bradyarrhythmias

The main cause of bradycardia and bradyarrhythmias in animals with neurological disease is brainstem compression (Cushing reflex). Brainstem compression causes sympathetic stimulation, which results in a marked increase in peripheral arterial BP. Initially, the heart rate also increases; however, the marked hypertension ultimately causes a reflex decrease in heart rate due to baroreceptor stimulation. Bradycardia may also occur secondary to drug overdose (e.g. opioid administration). Severe hypothermia and electrolyte abnormalities (hyperkalaemia and hypokalaemia) may also contribute to bradycardia in any critically ill patient.

Brainstem compression requires specific treatment to reduce ICP (diuretics, hyperventilation). (For details on specific management of increased ICP see Chapter 20.) Bradycardia secondary to opioid overdose requires a reduced dose of opioids +/- administration of reversal agents such as naloxone. Specific treatment of bradycardia requires administration of anticholinergics such as atropine. As these agents can mask the signs of brainstem herniation (e.g. pupil and heart rate changes), use of these agents in animals with intracranial disease needs to be performed carefully and increased ICP as a cause of the bradycardia needs to be ruled out before these agents are administered.

Poor myocardial contractility

Decreased cardiac muscle contraction most commonly occurs in neurological patients secondary to the use of anaesthetic and sedative drugs. Development of SIRS secondary to prolonged hypotension, hypoxaemia, ventilator-induced injury or multiple organ trauma may be another cause of reduced myocardial contractility in the neurological patient.

Improving myocardial contractility requires the identification and treatment of underlying causes. For drug-induced decreases in contractility, delivery of the agent needs to be decreased or stopped if possible. Use of multimodal anaesthesia with opioid-based protocols will reduce the requirement for the more cardiovascular and respiratory depressant anaesthetic drugs. The undesirable effects of anaesthesia can also be minimized by using short-acting agents that can be titrated to effect. (For more details of methods of reducing anaesthetic-related cardiovascular depression see Chapter 29.)

Inotropes are indicated when management of the underlying cause does not improve myocardial contractility or when urgent improvement in perfusion is required. Inotropes that can be used include dopamine (2–5 µg/kg/min) or dobutamine (2–5 µg/kg/min).

Obstructive shock

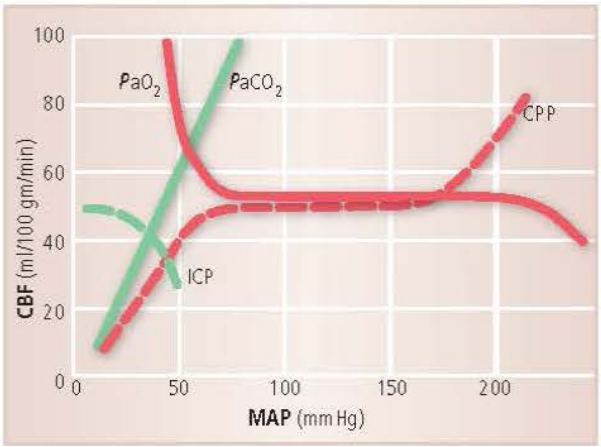
Obstructive shock occurs due to physical interference with venous return to the heart resulting in decreased preload and, therefore, stroke volume and cardiac output. In animals with trauma, obstruction to venous return may occur in association with pneumothorax. In these cases, prompt removal of the air by thoracocentesis or a chest drain will result in resolution of the shock.

Hypertension

Definition

In non-neurological patients, hypertension is defined as an MAP of >100 mmHg and a SAP of >150 mmHg. In neurological patients, increases in mean BP and, therefore, CPP outside the normal autoregulatory range of the brain cause linear increases in blood volume and ICP (**40**). In addition, abnormal brain tissue loses the ability to autoregulate. In these regions, any increase in mean BP is associated with an increase in cerebral blood volume and, potentially, an increase in ICP. Maintenance of a stable normal BP is therefore important in these animals to prevent increases in ICP.

▼ **40 Relationship between cerebral blood flow and intracranial pressure in response to changes in cerebral perfusion pressure, arterial carbon dioxide and oxygen tension. Normal pressure autoregulation of blood flow (dotted red line) maintains appropriate cerebral blood flow despite fluctuation in the mean arterial pressure. Increased $PaCO_2$ (green line) causes a global increase in cerebral blood flow that exceeds demand. Cerebral blood flow is unchanged until PaO_2 levels fall below approximately 60 mmHg, when it rises sharply.**



Causes of hypertension

As described above, MAP = CO × SVR. Cardiac output is dependent on heart rate and stroke volume, which in turn are dependent on preload, contractility and afterload. Therefore, an increase in any of these factors may increase BP. The extent of the increase will depend on the degree of compensation.

Causes of hypertension in neurological patients include peripheral vasoconstriction, tachycardia and hypervolaemia (increased preload). Peripheral vasoconstriction can occur due to increased ICP and brainstem compression (Cushing reflex) in animals with intracranial disease. Peripheral vasoconstriction, tachycardia and associated hypertension may also occur secondary to sympathetic stimulation caused by pain and anxiety.

Management

Specific management of increased ICP is detailed in Chapter 20. To minimize other causes of hypertension, adequate pain management and careful administration of fluids are important. Where hypertension persists despite correction of underlying causes, specific pharmacological treatment may be required to prevent detrimental effects on ICP and neurological function.

Persistent hypertension, despite adequate analgesia, can be treated by the administration of beta receptor antagonists or calcium channel blockers. Agents that have been used in human patients with head trauma include esmolol (β blocker), labetalol (mixed α and β blocker) and nicardipine (calcium channel blocker). Use of these agents in small animal neurological patients has not been reported. Esmolol is commonly used to treat tachyarrhythmias in small animals and labetolol has been described for use in a hypertensive crisis. Nicardipine is not used clinically in small animals at present; however, amlodipine, a calcium channel blocker used in small animals with cardiovascular disease, may be a suitable alternative. The dose rates of these agents can be found in critical care texts (see Further reading).

Sodium nitroprusside is also used in small animal patients with cardiac disease to control hypertension; however, this agent is best avoided in patients with neurological injury due to its risk of causing increases in ICP.

The use of any agent that decreases BP should be associated with close monitoring of BP to ensure excessive reduction and hypotension do not occur.

Monitoring the cardiovascular system

Arterial blood pressure

Arterial BP can be measured non-invasively using oscillometric or Doppler techniques (**41**). Oscillometric techniques (e.g. device for indirect non-invasive, automated, mean arterial pressure [DINAMAP]) provide automatic intermittent measurement of mean, systolic and diastolic pressure and pulse rate. The minimum amount of time between repeated measurements is 2 minutes. Many of the commercial systems available are unreliable in very small animals, such as cats, and in hypotensive or bradycardic patients. However, the accuracy in these situations is improving with newer equipment that is becoming more readily available. The Doppler technique is performed manually and is limited to measurement of SAP. However, this technique is more reliable in small animals and in shocked patients.

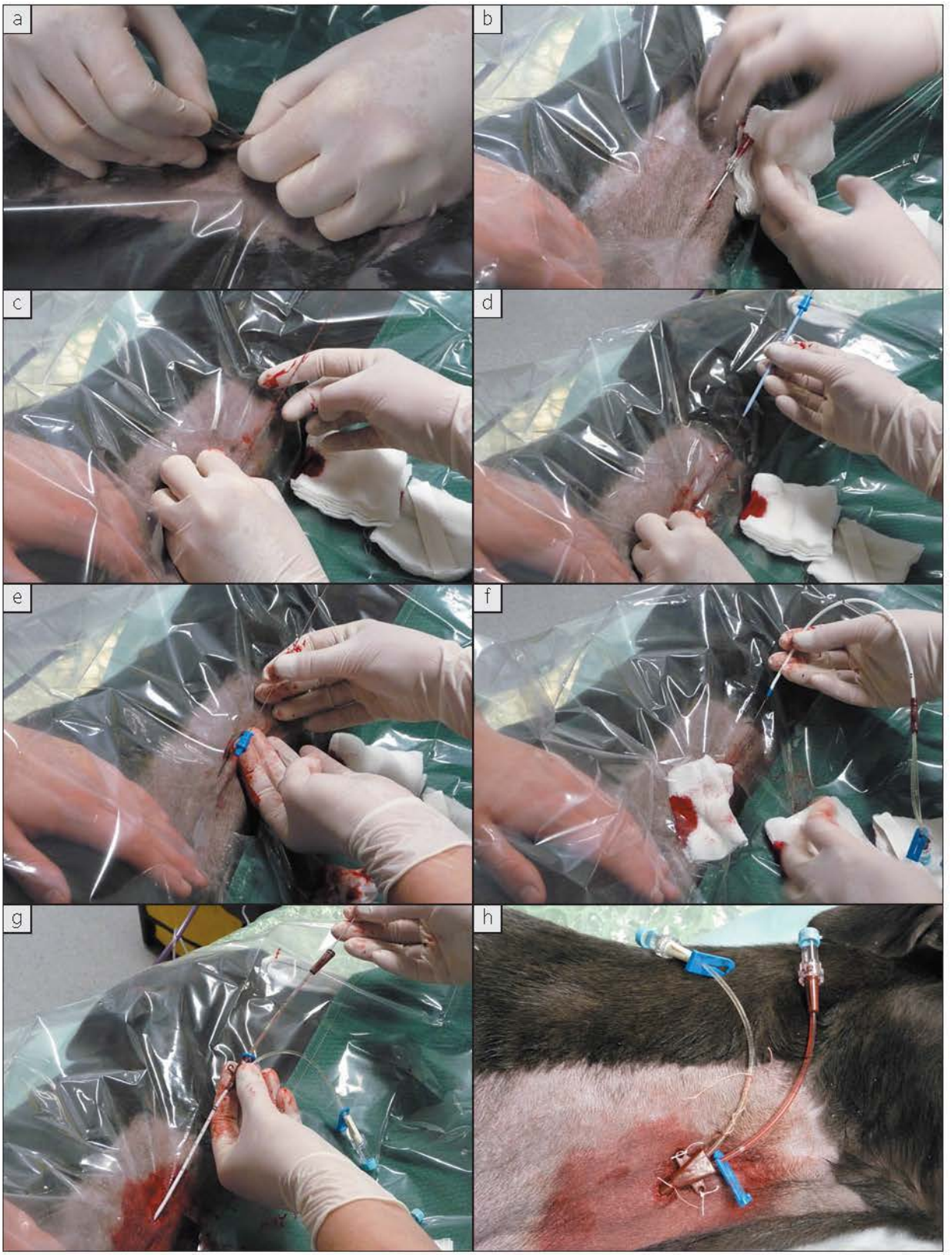
In unstable animals or chronically ventilated animals, invasive BP monitoring via an arterial catheter (**42**) is preferred over non-invasive methods. Invasive techniques allow continuous monitoring of BP. Catheters are most commonly inserted in the dorsal pedal artery in small animals. In addition, arterial blood gases can be obtained via the arterial catheter, allowing accurate assessment of pulmonary function and oxygen delivery.

▼ **41** The Doppler technique can be very useful for measuring blood pressure, particularly in small animals.



▶ **42** Arterial blood pressure is commonly measured directly via a catheter placed in the dorsal pedal artery. (a) Prior to placement, the hair over the medial surface of the dorsal tarsus is clipped and the site disinfected. (b) A small amount of lidocaine (2%) can be injected subcutaneously over the artery at the intended site of catheter insertion. This is particularly useful in conscious animals to prevent discomfort and movement during insertion. It can also be useful in anaesthetized animals as the vasodilation associated with the lidocaine administration can aid catheter placement. (c) Prior to catheter placement, a small stab incision can be made in the skin. This allows the catheter to be inserted with greater control as there is no longer any skin resistance. The artery is then gently palpated at the site of insertion and the catheter inserted gently but firmly in the direction of palpation. If the artery continues to be palpable as the catheter is inserted, then it is likely that the catheter is too far lateral or medial to the artery. If the artery cannot be palpated, the catheter may be between the artery and skin. A flash of blood will enter the hub of the stylet once the arterial wall has been penetrated by the bevel of the stylet. It is essential that the catheter is not separated from the stylet until at least 5 mm have been inserted to ensure that both stylet and catheter have penetrated the wall of the artery. If this has not occurred, the catheter will not be able to be inserted. (d) Taping and/or superglue can be used to secure the catheter in place. (e) The catheter can then be connected to the fluid line to allow blood-pressure monitoring.


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◀ **43** Insertion of a catheter into the jugular vein. Prior to placement, the dead space of the catheter is filled with saline or heparinized saline and an area over the selected jugular vein is clipped. The site is then disinfected. A roll of bandage or gauze placed under the neck can be useful for increasing visibility of the vein, but care should be taken not to occlude the dependent jugular vein in animals with intracranial disease. (a) A small stab incision can be made (carefully) in the skin over the jugular vein, as shown by tenting the skin between two fingers; this assists placement of the catheter. (b) With an assistant compressing the vein proximally, the introducer (a needle or catheter) is inserted through the stab incision into the jugular vein. (c) Once the guide wire has been placed, the needle introducer is removed, leaving the wire in place. (d) The dilator is then passed over the wire and threaded into the vein. (e) A gentle but firm twisting action will help insert the dilator through the skin and vessel wall. The dilator is them removed, again leaving the wire in place. At this stage some haemorrhage will occur at the entry site as the hole in the vessel wall is larger than the wire. Gentle pressure at the entry site using a sterile swab will reduce the amount of haemorrhage until the catheter is placed. (f) The catheter is then passed over the guide wire. During insertion of the catheter it is essential to maintain a hold on the guide wire at all times. The wire is inserted into the proximal end of the catheter and gradually passed up the catheter. (g) When the hub of the catheter is reached, the injection port is removed and the wire passed through the end of the catheter. Once the wire passes through the hub, the operator can hold the wire and pass the catheter over the wire into the vein. The wire is then removed and the injection port replaced. The catheter is flushed with saline. (h) The catheter is sutured in place. A sterile dressing is placed over the entry wound. Neck bandages should not be used in animals with intracranial disease, but can be used in other patients to help secure the catheter in place.

Central venous pressure

CVP is measured using a fluid-filled catheter inserted into the cranial vena cava via the jugular vein (**43**). Placement of the catheter in the jugular vein may increase the risk of disturbance to venous return and increased ICP. An alternative is to place a percutaneous central catheter, which is passed into the caudal vena cava via a catheter in the medial saphenous vein (**44**). Where this is not possible, a jugular venous catheter can be placed, taking care not to occlude the jugular during placement (surgical exposure may be required) and utilizing a catheter with as small a diameter as possible to minimize interference with venous return. The use of neck bandages over these catheters is discouraged in animals with intracranial disease.

CVP in spontaneously breathing animals is normally between 0 and 10 cm H_2O. CVP is determined by the amount of blood returning to the heart and the ability of the heart to pump this blood. Therefore, measurement of CVP will help differentiate cardiac and hypovolaemic causes of hypotension and determine appropriate treatment. A low BP accompanied by a high CVP suggests that the heart is unable effectively to pump blood returning to the heart, while low BP and CVP supports a reduction in the volume of blood returning to the heart (i.e. hypovolaemia). In contrast, a high CVP and high MAP would suggest hypervolaemia.

Measurement of CVP is helpful to determine the extent of adverse effects of ventilation. A high CVP can be caused by high mean intrathoracic pressure used for ventilation. In such a case, the PIP and/or PEEP requires adjustment.



► **44** Central venous pressure can be measured via a catheter placed in the caudal vena cava via the medial saphenous vein.

Urine output

Urine output provides an indirect indication of renal perfusion and therefore circulating blood volume and hydration status. It is an extremely valuable tool for assessing the adequacy of cardiovascular function in neurological patients.

Urine output is normally 1–2 ml/kg/hour in normovolaemic patients on normal maintenance fluid rates. Higher rates should be expected in normally hydrated animals receiving more than maintenance rates of fluid. Higher than normal output is also expected in animals that have received diuretics or glucocorticoids. (For more details on interpretation of changes in urine output see Chapter 31.)

Monitoring of urine output is easy, cheap and informative. An indwelling urinary catheter is inserted and a closed collection system set up. It is an extremely useful way of assessing fluid balance in unstable neurological patients, particularly those receiving diuretics, where fluid losses in the urine are higher than normal. In addition, animals with traumatic brain injury may have alterations in the reabsorption of renal sodium and water (e.g. central diabetes insipidus [DI] resulting in abnormal urine production and urine SG).

METABOLIC EVALUATION OF CRITICALLY ILL NEUROLOGICAL PATIENTS

Louise Clark

INTRODUCTION

When presented with a severely ill animal with primary neurological dysfunction it is important to consider any deleterious metabolic consequences that this disease may cause. The animal should be considered as a whole and thought given as to how the pathophysiology of the presenting disease may affect the systemic metabolic function.

In addition to a careful serial neurological evaluation, it is important that the whole animal is thoroughly assessed. The neurological presentation may be only part of the global presentation and underlying pathology. Consideration should be given to the presence of any co-morbidities (i.e. any other potentially unrelated pathology that may influence assessment, management and prognosis of the primary presenting neurological disease). This chapter will focus on how to utilize the information provided by bedside testing modalities, and the tests that might be more appropriate with specific neurological presentations.

GENERAL APPROACH

The history and clinical and neurological examinations will provide information to direct the clinician as to which tests are most appropriate for any particular case. Blanket testing is inappropriate, expensive and will not necessarily yield clinically relevant information. In any critically ill patient it is always appropriate to obtain a minimum database. The most useful information will be obtained from an assessment of packed cell volume/total protein (PCV/TP), a basic biochemical evaluation, including glucose plus electrolytes and acid–base analysis, and urinalysis. An evaluation of haematology, coagulation status and blood typing may also be appropriate. Further diagnostic testing and imaging may be indicated where there is polytrauma or where serious co-existing disease is suspected.

The relevant tests in critically ill neurological patients should include:

- Minimum database:
  - Complete blood count (CBC) (haematology) and examination of blood smears.
  - Serum biochemical (including electrolytes) analysis.
  - Urinalysis (including cytology).
- Bedside tests (where equipment is available):
  - Serum osmolality.
  - Acid–base status (lactate).
  - Tests of haemostasis.
  - Blood typing.
  - Other biochemical assays including ammonia.

Many cases of neurological dysfunction with a metabolic aetiology have significant and sometimes specific minimum database abnormalities (see Chapter 27). Many animals with disease restricted to the CNS do not present with specific minimum database findings; however, this information can be useful in detecting concurrent and potentially unrelated systemic disease and may direct further investigation. Infectious and sterile inflammatory disease processes demonstrate non-specific haematological changes and some biochemical abnormalities (see Chapter 19). Neoplastic and toxic disease processes may also manifest as haematological, biochemical and urinalysis changes. In the emergency patient with primary neurological disease, data from bedside tests can reveal abnormalities that require prompt treatment.

Packed cell volume and total protein

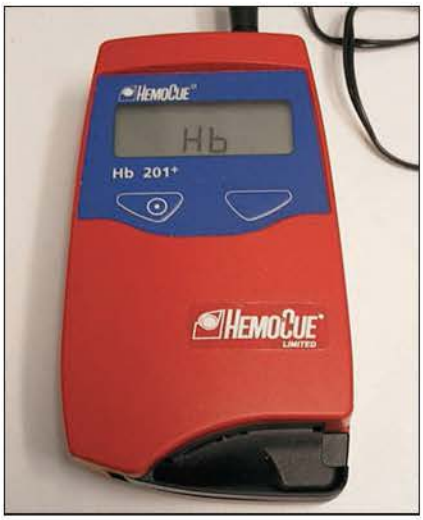
Fundamentals

Tissue oxygen delivery is reliant on an adequate circulating Hb concentration, cardiac output and tissue perfusion. Circulating Hb concentration can be directly measured at the bedside with a 'HemoCue' (**45**); however, in most clinical situations in veterinary medicine, PCV is determined by centrifugation of whole blood. Dividing the PCV (%) obtained by three gives an approximation of the circulating Hb (g/dl) concentration.

Assessment of PCV or Hb is mandatory. If the animal is presented immediately after trauma and significant haemorrhage, the PCV/Hb will not be reflective of actual oxygen-carrying capacity until the animal is adequately volume resuscitated. Splenic contraction may further complicate interpretation. Therefore, serial blood sampling may be appropriate.

An appropriate intervention threshold for transfusion might be higher than in most routine anaemia cases, which is generally a PCV of <0.2 l/l (20%). Mild haemodilution (PCV ~0.25 l/l [25%]) improves cerebral oxygen delivery by decreasing blood viscosity, but when PCV falls further, cerebral oxygen delivery may be compromised. Thus, in critically ill neurological patients the PCV should ideally be maintained above 0.2 l/l (20%). Where there has been significant haemorrhage, blood typing should be undertaken (see Chapter 31), and where there is any clinical suspicion of coagulopathy, a manual platelet count (blood smear) and coagulation evaluation are prudent. Where the PCV is low, a CBC, including blood smear, should always be performed in order to further characterize the anaemia.

Concomitant assessment of TP may be advantageous (**46**); there is some evidence that TP may fall more quickly than PCV in the presence of acute haemorrhage. Wherever haemorrhage is suspected or confirmed, serial PCV/TP evaluation is useful to evaluate the effects of fluid therapy and detect ongoing haemorrhage. Appropriate cardiovascular monitoring should also be established (see Chapter 2). TP may also be decreased in animals with severe hepatopathies, protein-losing nephropathies and protein-losing enteropathies. The presence of a low TP on bedside tests should direct further investigation. Conversely, the presence of dehydration may result in an artificially elevated PCV and TP and these findings should direct the clinician to re-evaluate the patient. (*Note:* TP elevation may also be identified when hyperglobulinaemia is present due to an infectious, immune-mediated or neoplastic aetiology.)



▲ **45** **HemoCue® for bedside analysis of haemoglobin concentration.**



◀ **46** **Refractometer for measurement of total solids (often considered equivalent to total protein) and urine specific gravity.**

Clinical relevance

The brain relies entirely on aerobic metabolism, and so it is very susceptible to hypoxic damage. It is therefore essential to maintain an adequate circulating Hb concentration in order to ensure adequate tissue oxygen delivery. The brain is especially vulnerable in cases of head trauma and raised ICP (due to any cause). Early correction of a low circulating Hb concentration will optimize oxygen delivery to the brain.

Plasma proteins play an important role in the maintenance of colloid osmotic pressure (COP) and, therefore, vascular volume, in addition to their other homeostatic functions. Hypoproteinaemic animals may be at risk from oedema formation and therefore fluid therapy must be tailored to their needs (see Chapter 31).

Testing

PCV and TP measurements are easily performed. Samples must be taken into the correct volume of anticoagulant and be spun for the appropriate duration, always ensuring that the refractometer is calibrated correctly. When there are concerns that a patient has raised ICP and blood tests are required, consideration should be given to sampling from a large intravenous catheter at the time of placement or from other peripheral veins. Jugular occlusion must be avoided when blood sampling. This applies to all the tests discussed below.

Normal ranges

Normal ranges will vary slightly according to the specific analyser and laboratory, but the following are guidelines:

- Canine: PCV, 0.37–0.55 l/l (37–55%); TP, 54–71 g/l (5.4–7.1 g/dl).
- Feline: PCV, 0.25–0.45 l/l (25–45%); TP, 60–86 g/l (6.0–8.6 g/dl).

Monitoring

Daily assessment of PCV and TP is appropriate in critically ill patients. Serial blood samples may be required for an assessment of the response to volume resuscitation or where ongoing haemorrhage is suspected.

Treatment

Fluid therapy and transfusion medicine are addressed in Chapter 31.

Glucose

Fundamentals

Normoglycaemia is maintained by a balance between the glucose-lowering hormone insulin and the glucose-elevating hormones glucagon, cortisol, epinephrine (adrenalin) and growth hormone.

Clinical relevance

The brain is an obligate consumer of glucose. Inadequate glucose supply to the brain (neuroglycopaenia) can lead directly to CNS signs. These include altered mentation, weakness and recumbency, ataxia, alterations in vision and seizures. Pacing, restlessness and vocalization may be evident prior to neurological signs; however, these are not consistent signs. There is some evidence that chronic hypoglycaemia, such as experienced in insulinoma cases, may result in upregulation of cerebral glucose uptake and a lack of neurological signs associated with hypoglycaemia. Hyperglycaemia may result in neurological signs and severe hyperglycaemia may manifest as hyperglycaemia–hyperosmolar syndrome, a complication of diabetes mellitus (see Chapter 27). Mild hyperglycaemia is common in cats presented as neurological emergencies; this is a manifestation of the stress response. Hyperglycaemia may also be documented in dogs, secondary to catecholamine release. In people, hyperglycaemia immediately after hypoxic–ischaemic injury causes damage to brain cells, and in acute cerebrovascular accidents, hyperglycaemia is associated with larger infarct volumes and a poorer prognosis. Hyperglycaemia has been documented in veterinary species following head trauma and the degree of hyperglycaemia is associated with the severity of the trauma. The significance of this finding is yet to be determined. However, because hyperglycaemia may potentiate neurological injury, it is prudent to avoid iatrogenic hyperglycaemia in patients with head trauma. Although there is a growing consensus amongst intensive care unit (ICU) clinicians working with human patients that maintaining normoglycaemia improves outcome, this topic remains controversial, especially as to the degree of glycaemic control required. Currently, no guidelines exist in veterinary practice. The use of soluble insulin to achieve normoglycaemia comes with a significant risk of inducing iatrogenic hypoglycaemia.

Testing

Hand-held portable glucometers are available with species-specific (canine and feline) software (**47**).

Normal ranges

The normal ranges for blood glucose will vary slightly between laboratories:

- Canine: 3.6–6.2 mmol/l (65–112 mg/dl).
- Feline: 3.7–9.3 mmol/l (67–167 mg/dl).

Neurological signs may be seen when blood glucose is <2.5 mmol/l (45 mg/dl) or >33.3 mmol/ (600 mg/dl) and associated with hyperosmolar syndrome. Some reports suggest that plasma glucose of 55.5 mmol/l (>1,000 mg/dl) may be associated with overt neurological signs.



▲ **47** Glucometer validated for use in cats and dogs.

Monitoring

The frequency of blood glucose monitoring will be determined by the underlying disease process. More details are given in Chapter 27.

Treatment

Hypoglycaemia should be treated as an emergency. Initial treatment is usually symptomatic (1 ml/kg of 50% [0.5 g/kg] dextrose/glucose diluted to a 5–10% solution and administered slowly IV). (*Note:* This solution is hypertonic and can cause thrombophlebitis.) The response to treatment should be carefully monitored by serial glucose evaluation and, more importantly, by clinical signs. A constant rate infusion (CRI) of 2.5–5% dextrose/glucose, preferably in an isotonic crystalloid such as 0.9% NaCl, can then be administered. Where solutions of concentration >5% are necessary, they should be given through a central line to reduce the incidence of thrombophlebitis. Five percent glucose/dextrose in water should not be used for bolus administration; it may cause acute decreases in osmolality and cerebral oedema. (*Note:* The ongoing glucose supplementation can result in a tendency toward hypokalaemia.) If appropriate, oral glucose administration should be considered. Glucagon CRIs may be appropriate for animals with confirmed insulin or insulin-like peptide-secreting tumours. It is not clear whether a 'lone' elevated glucose level should be treated. (*Note:* This situation does not apply to hyperglycaemic hyperosmolar syndrome or to diabetic ketoacidois, which should be treated as an emergency.)

Electrolytes

Fundamentals

The primary electrolytes that are considered relevant in disease processes in the neurological patient are sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), magnesium (Mg^{2+}) and chloride (Cl^-). Bicarbonate (HCO_3^-) is addressed later in this chapter (p. 70). There is a subtle and complex electrolyte balance between the intracellular and extracellular compartments. Electrolytes may enter or leave the cell membrane through various ion channels. The maintenance of osmotic gradients of electrolytes is important. Such gradients affect and regulate the hydration of the body and blood pH, and are critical for nerve and muscle function. Various mechanisms exist in living species that keep the concentrations of different electrolytes under tight control. The major extracellular ions are Na^+ and Cl^-. The major intracellular ions are K^+ and Mg^{2+}.

Clinical relevance

Metabolic causes of neurological disease are considered in Chapter 27. There are several primary neurological diseases that may manifest with electrolyte abnormalities and the aetiology, clinical significance and management are briefly discussed below.

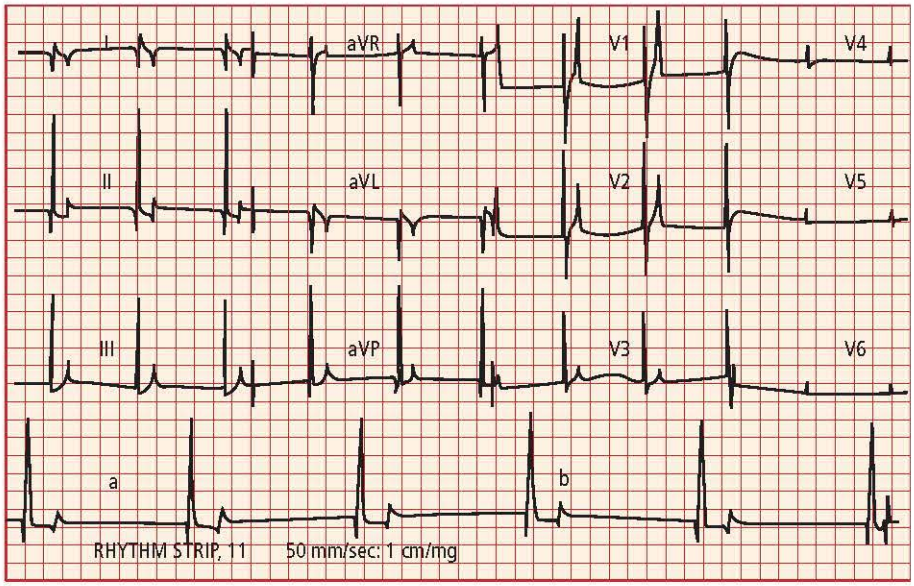
Hyperkalaemia

In the context of neurological emergencies, hyperkalaemia is most likely to occur in an animal that has suffered polytrauma and urinary tract rupture. Uroabdomen may result in profound dehydration and hypovolaemia, life-threatening hyperkalaemia, severe azotaemia, chemical peritonitis and metabolic acidosis. Hyperkalaemia is immediately life threatening because it affects the depolarization of cardiac myocytes. Clinical signs include inappropriate bradycardia. In particular, cats may not be truly bradycardic, but their heart rate is inappropriately low for their stressed situation. An immediate electrocardiogram (ECG) is required (**48**). Classical ECG changes seen with hyperkalaemia include T-wave changes, bradycardia and atrial standstill progressing to asystole. Wide complex (ventricular) tachycardias are also possible. (*Note:* Some animals can be severely hyperkalaemic without obvious ECG changes.)

In any case where the K^+ concentration is >7 mmol/l (mEq/l), and particularly if this is accompanied by ECG changes, calcium administration is indicated. In the first instance, 10% calcium gluconate can be administered (0.5–1.0 ml/kg over about 10 minutes). This will restore the 'normal' gap between the resting membrane potential and threshold potential of cardiac cells and reduce the risk of cardiac arrhythmias. However, it will not alter extracellular potassium concentrations and is only effective for up to 1 hour.

There are several ways of reducing extracellular potassium concentrations, either by driving K^+ into cells or increasing K^+ excretion. Multiple strategies may be required in the severely hyperkalaemic patient:

- Volume expansion with crystalloids (usually NaCl 0.9% because this contains no K^+) aims to resolve any underlying acidosis (acidosis potentiates hyperkalaemia), dilute the K^+ and also promote K^+ excretion by diuresis.
- Dextrose/glucose saline infusion causes endogenous insulin release, and insulin drives K^+ into cells. NaCl 0.9% with 5% dextrose will also promote volume expansion. Hypotonic glucose-containing fluids (e.g. NaCl 0.18% with 4% glucose) do not contribute to volume resuscitation. In practice this approach may result in insufficient insulin release to reduce serum K^+.
- Regular (soluble) insulin (0.2–0.5 IU/kg IV), followed by 2 g dextrose (4 ml of 50% dextrose) per unit of insulin administered and then a 2.5–5% dextrose infusion. Concentrations of dextrose or glucose in excess of 5% can cause thrombophlebitis and it should be administered via a central catheter. It is prudent to evaluate glucose and K^+ concentrations every 15–20 minutes for the first hour to ensure efficacy of treatment and to avoid iatrogenic hyperglycaemia or hypoglycaemia.



◀ 48 ECG demonstrating hyperkalaemia in a dog. ECG findings may include the following: a reduction in P-wave amplitude and prolongation of PR interval to complete absence of P waves (a); increase in QRS duration; increase in QT duration (b); slowing of the heart rate; T waves become tall and spiked; decreased R-wave amplitude.

- Bicarbonate (1–2 mEq/kg IV slowly over 15 minutes). Bicarbonate is hyperosmolar and should be diluted according to the manufacturer's instructions. This approach relies on the patient being able to remove (by ventilation) the additional CO_2 produced. It should not be used in patients with respiratory compromise or a pre-existing metabolic alkalosis.
- Administration of all K^+-containing fluids or nutrition and any drugs that promote hyperkalaemia (e.g. spironolactone, angiotensin-converting enzyme [ACE] inhibitors) should be stopped.

Hypernatraemia

Normal animals deprived of water for considerable periods of time can become severely hypernatraemic. Loss of low-sodium fluid through vomiting, diarrhoea or polyuria may also cause hypernatraemia. In the primary neurological patient the most common cause of hypernatraemia is probably central diabetes insipidus, which may occur secondary to traumatic brain injury or pituitary masses and has been reported in granulomatous meningoencephalitis, hydrocephalus and CNS lymphoma.

Iatrogenic hypernatraemia can result from excess NaCl administration, either orally or via IV fluids (e.g. hypertonic saline or sodium bicarbonate). Serum sodium levels in excess of 180 mmol/l (mEq/l) may be associated with neurological signs such as head pressing and stupor and progressing to coma, seizures and death. Hypernatraemia causes free water to move out of the cell into the relatively hyperosmolar extracellular space, leading to a decreased cell volume. This results in the formation of intracellular osmolytes in order to replenish cell volume; complete compensation can take 24 hours. These osmolytes must be considered during the management of hypernatraemia.

Patients with hypernatraemia have a free water deficit and should be managed as such, aiming to reduce serum sodium by no more than 0.5 mmol/l/hour (mEq/l/hour). Rapid drops in plasma sodium concentration (and therefore osmolality) cause a rapid movement of free water back into the intracellular space. Overly rapid correction will result in cellular swelling (i.e. neuronal oedema) because the osmolytes are broken down relatively slowly. Further details on the management of hypernatraemia can be found in Chapter 27.

Hyponatraemia

Hyponatraemia is relatively uncommon in critically ill dogs and cats, but neurological patients with head trauma or intracranial masses, particularly pituitary lesions, may be predisposed. Dogs and cats with hyponatraemia almost always have free-water retention rather than an absolute sodium deficit. When serum sodium falls below 120 mmol/l (mEq/l) or falls rapidly, clinical signs may be evident. These include obtundation, seizures, head pressing, coma and death.

Hyponatraemia by itself produces brain oedema because it causes free-water to move into the relatively hyperosmolar cell. This may result in increased ICP, with potential neuropathological sequelae. When serum sodium decreases, the brain prevents further cellular swelling by extruding intracellular electrolytes and organic osmolytes, a process that is almost fully achieved after 48 hours. Conversely, during the subsequent increase in serum sodium, re-establishment of intracerebral osmolytes occurs, but their reuptake is more delayed (+/- 5 days). Rapid or excessive correction of this hyponatraemia can be followed by development of brain demyelinating lesions (central pontine myelinolysis, also known as osmotic demyelination syndrome). This is a result of neuronal shrinking as water moves out of the cell during correction of hyponatraemia (i.e. as extracellular osmolality increases, water is drawn into the extracellular space). Guidelines suggest that sodium should not be corrected at a rate greater than 0.5 mmol/l/hour (mEq/l/hour). Further details on the treatment of hyponatraemia can be found in Chapter 27.

Testing

There are both wet and dry chemistry analysers available that can determine electrolytes. EDTA contamination and red cell haemolysis must be avoided to prevent apparent hyperkalaemia. Excess heparin may result in apparent hypocalcaemia. Animals receiving potassium bromide may demonstrate an apparent hyperchloraemia dependent on the type of analyser used.

Normal ranges

See *Table 10*.

Table 10 **Typical electrolyte composition of extracellular and intracellular fluids**

Electrolyte	Extracellular fluid (mmol/l)*	Intracellular fluid (mmol/l)*
Na^+	140–150	10
K^+	3.5–5.0	141
Ca^{2+}	1.5	<1
Mg^{2+}	3	50
Cl^-	106–120	4
HCO_3^-	19–25	10

Other ions not included

* mmol/l = mEq/l for univalent ions

Monitoring

During the correction of hyponatraemia, serum sodium should be monitored every 1–2 hours and during the correction of hypernatraemia at least every 4 hours. Where animals are hyperkalaemic, monitoring may be required every 30 minutes initially in order to establish that there is an appropriate response to treatment and that the serum potassium level is falling below that considered to be life threatening.

Treatment

See Chapter 27 for the treatment of metabolic diseases and Chapter 31 for the treatment of hyponatraemia.

Urinalysis

Fundamentals

Bedside urinalysis tests include urine SG (USG) and a dipstick. Cytology, culture and further tests, including urine protein:creatinine ratio, may be indicated in the diagnosis and management of specific diseases. Urine volume depends on hydration status and renal concentrating ability and is inversely related to the USG. Urine concentration will affect the depth of the colour. Cloudy red urine that clears after centrifugation is seen when RBCs (haematuria) are present. Dark red to brown colour may be due to haemoglobinuria or myoglobinuria. Yellow-brown, greenish-yellow or dark brown urine may be due to bilirubinuria. Other urine colours may result from certain drug therapies.

Urine is normally clear. Semen, mucus and lipid may cause turbidity in normal urine. Increased numbers of cells, crystals, casts or organisms can increase the turbidity of urine in disease conditions. An unpleasant odour may indicate sepsis. Animals with ketosis/ketoacidosis may have urine with an acetone odour.

Clinical relevance

Urinalysis in conjunction with USG is a useful indicator of renal perfusion and volume status in an animal with previously normal renal and endocrine functions. An elevated USG and a low urine output suggest hypovolaemia (see Chapter 31). USG may also provide additional information to support a diagnosis of endocrine disease. Dogs with Cushing's syndrome and central or nephrogenic DI are often hyposthenuric (can be isosthenuric). Central DI may occur with pituitary neoplasia or after head trauma or craniectomy. Secondary nephrogenic DI is very common and is caused by a failure of the kidney to respond to vasopressin (*Table 11*). Other differential diagnoses that must be considered when USG is inappropriately low include chronic renal failure and ethylene glycol toxicity, which also results in the formation of calcium oxalate monohydrate crystals. (*Note:* Many drugs, including steroids, diuretics, phenobarbital and alpha 2 agonists, can have effects on USG.)

Differentials for myoglobinuria include seizures, crush injuries and severe muscle disease (e.g. necrotizing myopathy).

Table 11 **Common causes of secondary nephrogenic diabetes insipidus**

Disease process
• Gram-negative sepsis including pyometra
• Hypercalcaemia
• Hypokalaemia
• Pyelonephritis
• Portosystemic shunts and liver failure
• Hypoadrenocorticism (dogs)
• Hyperthyroidism (cats)

Testing

Urine samples obtained by catheterization may have red cell, epithelial cell, lubricant and bacterial contamination. Free catch samples are also non-sterile. Cystocentesis samples may contain red cells, but are indicated where urinary culture is required. Urine is unstable and must be analysed promptly. It should be collected in clean or sterile containers and, if not analysed within a short period of time, it should be refrigerated. Cold urine should be allowed to return to room temperature prior to analysis to avoid a false increase in SG. Precipitates may form in urine as it cools, and cold may interfere with some chemical tests. Refractometers must be calibrated prior to use.

Dipstick analysis

Dipsticks are labile. They must be kept dry, in well-capped jars and used prior to the expiration date for accurate results. Prolonged exposure to air may cause false-positive tests for glucose and false-negative tests for occult blood.

Urine pH

Acidic urine is caused by increased acid excretion or production (increased protein catabolism, metabolic or respiratory acidosis, paradoxical aciduria with alkalosis). Alkaline urine is caused by increased alkali excretion or production (decreased protein catabolism, cystitis due to urea-splitting bacteria, prolonged storage at room temperature, metabolic or respiratory alkalosis). Urine pH is not an accurate indicator of systemic acid–base balance.

Protein

Urine protein results must always be interpreted in conjunction with SG. A small amount of protein is normally present in urine and may be detected in concentrated urine. Many false-positive protein tests occur, especially with alkaline urine. The protein test mainly detects albumin on the dipstick. Physiological pre-renal proteinuria may result from excessive muscular exertion, convulsions or excess protein ingestion. Pathological proteinuria may be pre-renal (haemoglobinuria, myoglobinuria), renal (glomerular or tubular) or post-renal (urogenital haemorrhage or inflammation).

Glucose

Glucose in urine, an abnormal finding, occurs when blood glucose levels exceed the renal threshold for reabsorption. Glucosuria with hyperglycaemia occurs in diabetes mellitus, following dextrose administration or secondary to catecholamines or glucocorticoids. Glucosuria without hyperglycaemia may occur when hyperglycaemia is transient or in selective renal proximal tubule dysfunction. Urine containing glucose is an excellent culture medium for bacteria.

Ketones

Ketonuria occurs when ketone production exceeds the renal tubular absorption capacity. Dipsticks are semi-quantitative only. The urine ketone test detects aceto-acetate, but not beta hydroxybutyrate. False-positive test results may occur if urine is highly pigmented. False-negative results are uncommon in fresh urine, but may occur when urine has been standing due to the volatility of ketones. Ketonuria may occur in diabetic ketoacidosis, pregnancy, ketosis, insulinoma, glycogen storage disease or starvation.

Haemoprotein (occult blood)

Haemoproteinuria may result from increased RBCs (haematuria, especially dilute urine with lysed RBCs), haemoglobinuria or myoglobinuria. Sediment evaluation may differentiate haematuria from haemoglobinuria and myoglobinuria. Typically, red urine supernatant indicates haemoglobin or myoglobin. Haemoglobinuria is often accompanied by haemoglobinaemia.

Bilirubin

Dogs with concentrated urine may have trace to 1+ bilirubinuria; they have a lower renal threshold for bilirubin than do other species, and canine renal epithelium can also conjugate and excrete bilirubin (especially in male dogs).

Urobilinogen

Testing for urobilinogen in the urine should not be relied on in dogs and cats.

Normal ranges

USG is one of the most important tests in a urinalysis and should be done using refractometry. (*Note:* Do not use dipstick tests for SG.) Turbidity of the urine can affect the SG (usually increases it). Ideally, urine should first be centrifuged and the supernatant used for determination of SG. Normal SG values vary widely (usually between 1.015 and 1.045, up to 1.065+ in cats) depending on hydration status and water intake.

Cat urine contains different solutes from dog urine, therefore some refractometers have separate scales for cat urine to adjust for this. SG must be evaluated in light of the blood urea nitrogen (BUN)/creatinine values and hydration status. Abnormal substances, such as glucose and proteins, may falsely increase the SG.

Monitoring

A single sample may be adequate in some disease processes. In contrast, urine output and USG may be measured every 1–4 hours in an animal that is severely hypovolaemic and receiving fluid therapy. In an animal that has had a craniectomy and is receiving multiple drugs, including steroids, serial electrolyte and USG evaluation should be performed in the period following surgery.

Treatment

Urinalysis findings always reflect the underlying disease process. It is important not to treat the urinalysis findings themselves, but to establish what the underlying disease process is. Extensive guidance on fluid therapy can be found in Chapter 31.

Serum osmolality

Fundamentals

Serum osmolality is the determinant of osmotic pressure, which determines movement of water in and out of cells, therefore clinically it is an indicator of electrolyte abnormalities, renal function, etc. In the majority of cases, sodium disorders in cats and dogs result from abnormalities in water handling rather than a change in the number of sodium ions. Plasma sodium concentration is the major determinant of plasma osmolality. An osmole is one mole of any fully dissociated substance dissolved in water.

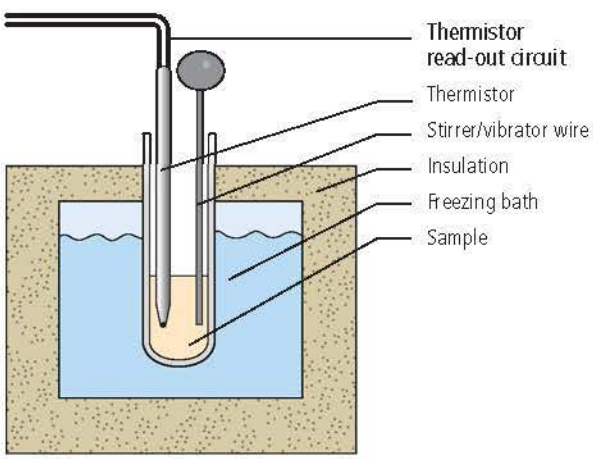
- **Osmolarity.** Osmotic concentration of a solution expressed as osmoles of solute per litre (i.e. volume) of solution.
- **Osmolality.** Osmotic concentration of a solution expressed as osmoles of solute per kg (i.e. mass) of solution.
- **Oncotic pressure.** A small portion of the total osmotic pressure that is due to the presence of large protein molecules.
- **Hyperosmolarity.** Increase in the osmolarity of a solution to above the normal plasma concentration.
- **Hypertonicity.** Ability of a hyperosmolar solution to redistribute fluid from the intra- to the extracellular compartment. Urea, for example, may be hyperosmotic, but because it equilibrates rapidly across membranes, it is not hypertonic.

Clinical relevance

Serum osmolality is a useful preliminary investigation for identifying the cause of hyponatraemia and may be useful in the assessment of fluid therapy (see Chapter 27). Assessment of the osmolar gap may be useful in identifying toxicity caused by hyperosmolar compounds such as ethylene glycol. Urine osmolality is an important test to evaluate the concentrating ability of the kidney.

Testing

Clinical measurement of osmolality requires a cryoscopic (freezing point) osmometer (**49**). This is a relatively expensive instrument, but convenient, rapid and easy to use.



▲ **49** **The cryoscopic osmometer uses the principle of freezing point depression to assess the number of osmoles present in a serum sample.**

If it is not possible to measure osmolality, the following equation can be used to estimate osmolarity:

Plasma osmolarity (mOsm/l) = (2 × serum Na [mmol/l]) + urea (mmol/l) + glucose (mmol/l)

or

Plasma osmolarity = (2 × serum Na [mEq/l]) + (BUN [mg/dl]/2.8) + (glucose [mg/dl]/18)

The doubling of sodium accounts for the negative ions associated with sodium and the exclusion of potassium allows approximately for the incomplete dissociation of sodium chloride. The difference between the measured osmolality and calculated plasma osmolarity is known as the osmolar gap; this is normally between 0 and 10 mOsm/kg (osmolar gap = osmolality – osmolarity). An elevated osmolar gap suggests the presence of osmotically active agents in the plasma (e.g. mannitol or ethylene glycol).

The following should be noted:

- There are several equations available in the literature to calculate osmolarity.
- The terms osmolarity and osmolality are used interchangeably in much of the medical literature.
- The units of osmolality (mOsm/kg) and osmolarity (mOsm/l) are different, so strictly they cannot be subtracted from one another. The value of the difference is clinically useful, so this problem is ignored.

Normal ranges

The normal range of plasma osmolarity is 285–295 mOsm/l.

Monitoring

Where hyperosmolar therapy is used, some authors quote an outcome goal for osmolarity: 300 mOsm/l or an Na^+ of 145–155 mmol/l (mEq/l). Increasing plasma osmolarity to >320 mOsm/l with hypertonic fluids (e.g. mannitol) should be avoided, as this has been associated with acute renal failure. When correcting acute, severe hyponatraemia, serial osmolality measurements may also be useful.

Acid–base status and blood gas analysis

Fundamentals

Normal electrolyte concentrations and acid–base equilibrium are important for normal neuronal function. Evaluating these parameters is useful for assessing the metabolic and respiratory status of a patient. While arterial samples are required for accurate assessment of respiratory function, venous samples are sufficient for assessment of metabolic disorders. Samples must always be anaerobically collected, heparinized and analysed immediately (or stored on ice).

Clinical relevance

Blood gas evaluation is the 'gold standard' for assessing respiratory function and arterial blood gas analysis is the only available method of assessing PaO_2. Mild to moderate hypoxaemia is often encountered in animals with thoracic trauma or other lung pathology. It is essential to maintain arterial oxygen content in order to maintain tissue oxygen delivery. Hypoventilation may occur in animals with neuromuscular disease and in those with head trauma or high cervical injury.

Any disease process that causes hypoperfusion (e.g. shock) may result in lactate accumulation and a metabolic acidosis. Early recognition of these metabolic abnormalities allows early and appropriate treatment.

Testing

Systematic approach to blood gas analysis

- Acidosis: an abnormal process or condition, which would lower arterial pH if there were no secondary changes in response to the primary aetiological factor.
- Alkalosis: an abnormal process or condition, which would raise arterial pH if there were no secondary changes in response to the primary aetiological factor.
- Simple (acid–base) disorders are those in which there is a single primary aetiological acid–base disorder.
- Mixed (acid–base) disorders are those in which two or more primary aetiological disorders are present simultaneously.
- Acidaemia: arterial pH <7.36.
- Alkalaemia: arterial pH >7.44.

A step-by-step overview on how to interpret blood gas samples is described below.

***Step 1:* Check arterial pH**

Any increase in H^+ ions will decrease pH. The net deviation in pH will indicate whether an acidosis or an alkalosis is present (but will not indicate mixed disorders). pH changes can be produced by metabolic or respiratory changes. Changes produced by one component will be opposed by the other. For example, to compensate for respiratory acidosis (secondary to hypoventilation) the organism will attempt to increase the HCO_3^- in the blood.

If an acidaemia is present, an acidosis must be present. If an alkalaemia is present, an alkalosis must be present. If pH is normal, either no acid–base disorder or a compensating disorder (i.e. a mixed disorder with an acidosis and an alkalosis) is present.

***Step 2:* What is happening with ventilation and metabolic indices? Look for a suggestive pattern in pCO_2 and HCO_3^-**

Each of the simple disorders produces predictable changes in pCO_2 and HCO_3^-.

If both HCO_3^- and pCO_2 are low, this suggests the presence of either a metabolic acidosis or a respiratory alkalosis (a mixed disorder cannot be excluded). If both HCO_3^- and pCO_2 are high, this suggests the presence of either a metabolic alkalosis or a respiratory acidosis (a mixed disorder cannot be excluded). If HCO_3^- and pCO_2 move in opposite directions, a mixed disorder must be present. Which disorder is present is dependent on which change is primary and which is compensatory, and this requires an assessment based on the history, examination and other results. Primary metabolic acidosis due to hypoperfusion or seizures (with respiratory compensation) and respiratory acidosis due to hypoventilation (with minimal compensation) are the most likely acid–base derangements in neurological emergency patients. Even with maximum compensation, the pH usually moves in the same direction as the primary problem (i.e. the body does not usually overcompensate for an acid–base disturbance).

***Step 3:* Check for evidence of specific disease in the other biochemistry results, especially electrolytes**

Certain disorders are associated with predictable changes in other biochemistry results (see above). For example, an animal with head trauma and severe volume depletion from haemorrhage is likely to have a primary metabolic acidosis with (or without) respiratory compensation. Routine haematological and biochemical evaluation is likely to demonstrate a pre-renal azotaemia and possibly a fall in PCV and a decreased TP. USG is likely to be very high and little urine will be produced.

***Step 4:* One problem or many?**

The appropriateness of the compensatory response should be assessed. A full discussion of compensatory responses is beyond the scope of this chapter, but can easily be obtained from other sources. Essentially, each abnormality (e.g. acute respiratory acidosis) will result in an expected compensation. In this case, HCO_3^- increases by 0.1 mmol/l (0.1 mEq/l) for every 1 mmHg change in pCO_2.

If the expected (having worked out the compensation) and actual values match, this implies no evidence of a mixed disorder. If the expected (having worked out the compensation) and actual values differ, this implies a mixed disorder is present.

***Step 5:* What is happening with oxygenation?**

PaO_2 is a very useful parameter, but it is dependent on the PAO_2. Adequate oxygenation requires a PaO_2 of >80 mmHg. Generally, PaO_2 should be within 10 mmHg of PAO_2 in a conscious animal breathing room air. Oxygenation is considered in more detail in Chapter 2.

***Step 6:* Formulate the acid–base diagnosis**

It is imperative that blood gas samples are collected anaerobically into the correct amount of anti-coagulant and analysed immediately or stored on ice (for 2 hours). Sampling errors are a common cause of misdiagnosis of blood gas abnormalities (see *Table 12*). (*Note:* A clinical assessment is vital to ensure that the assessment of blood gas analysis 'makes sense' and fits with the clinical diagnosis.)

Table 12 Common acid–base abnormalities in neurological patients

Respiratory acidosis

- Central respiratory depression (e.g. raised ICP/ head trauma)
- Neuromuscular disease (e.g. myasthenia gravis, botulism, polyradiculoneuritis, tick paralysis)
- Pleural space disease/chest wall disruption – secondary to trauma, diaphragmatic hernia
- High cervical spinal coral injury

Respiratory alkalosis

- Excessive mechanical ventilation
- Pulmonary thromboembolism
- Pulmonary oedema
- Pneumonia
- Pneumothorax/haemothorax
- Heat stroke
- Corticosteroid therapy
- Pain and anxiety
- Pyrexia
- Compensation for metabolic acidosis (e.g. in hypovolaemic shock or sepsis)

Metabolic acidosis

- Lactic acidosis (see *Table 14*)
- Hyperchloraemic – excess 0.9% NaCl administration
- Ketoacidosis (diabetes)

Metabolic alkalosis

- Hypoalbuminaemia – sepsis/systemic inflammatory response syndrome
- Diuretic use
- Gastric vomiting

Table 13 Normal ranges for blood gas analyses

PARAMETER	DOG	CAT
pH	7.39 ± 0.03	7.39 ± 0.08
$PaCO_2$ (mmHg)	37 ± 3	31 ± 6
PaO_2 (mmHg)	102 ± 7	107 ± 12
HCO_3^- (mmol/l)	21 ± 2	18 ± 4
Base excess (mmol/l)	2 ± 2	2 ± 2

Normal ranges

See *Table 13*.

Monitoring

Blood gas equilibrium is a dynamic equilibrium and reassessment may be appropriate to gauge response to therapy. The frequency of measurement will be determined by the severity of disease. A venous blood gas sample taken on admission and shown to be normal may be adequate in some patients. In comparison, an animal with tetanus on a ventilator should have arterial blood gases checked approximately every half hour in the initial stabilization period. Pulse oximetry and capnography may then be used for monitoring, with blood gases being performed every 4–6 hours.

Treatment

Treatment of acid–base abnormalities should always be directed at the underlying cause; the aetiology of the disease process will guide the clinician appropriately. Treatment of respiratory acidosis is also considered in Chapter 2.

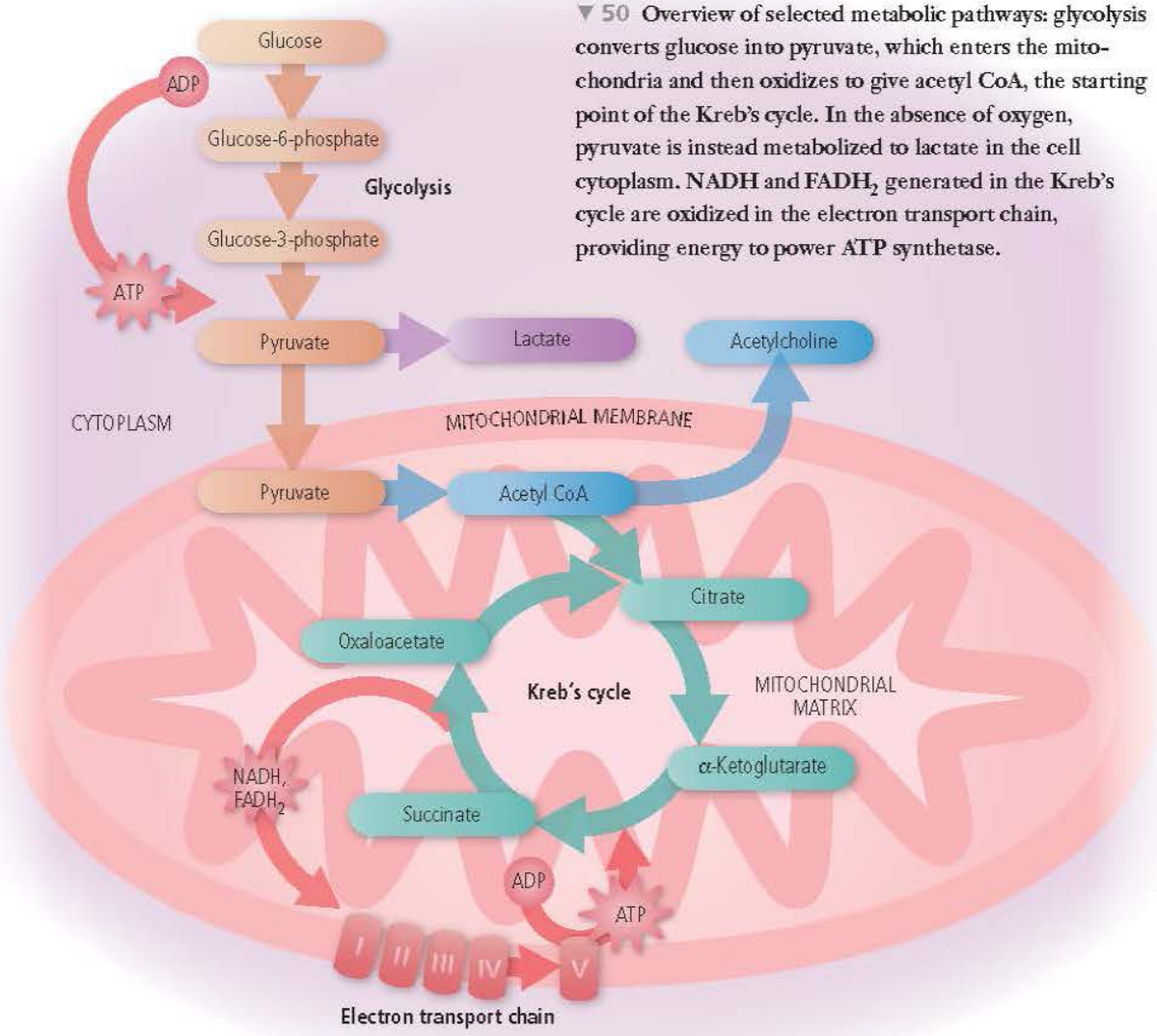
Lactate

Fundamentals

Lactate is a by-product of anaerobic glycolysis. Glucose is broken down into pyruvate by the glycolytic pathway and, in the presence of sufficient oxygen, is able to enter the Kreb's cycle and electron transfer chain situated in the mitochondria (**50**). In the absence of oxygen, pyruvate does not enter the Kreb's cycle; to maintain glycolysis and limited adenosine triphosphate (ATP) production, it is metabolized in the cytoplasm to lactate. The liver then clears more than 50% of blood lactate, while the kidneys and muscles metabolize the remainder. Thiamine is a necessary cofactor of pyruvate dehydrogenase, which turns pyruvate into acetyl coenzyme A before it enters the Kreb's cycle. Thiamine deficiency can therefore potentiate problems with lactate metabolism.

Clinical relevance

Lactic acidosis is essentially a form of metabolic acidosis, caused by an excess of lactic acid in the cells and circulation. There are major adverse consequences of severe acidaemia, which affect all body systems, and there is an associated increased mortality in critically ill human patients with a raised lactate concentration.



▼ 50 **Overview of selected metabolic pathways: glycolysis converts glucose into pyruvate, which enters the mitochondria and then oxidizes to give acetyl CoA, the starting point of the Kreb's cycle. In the absence of oxygen, pyruvate is instead metabolized to lactate in the cell cytoplasm. NADH and $FADH_2$ generated in the Kreb's cycle are oxidized in the electron transport chain, providing energy to power ATP synthetase.**

Lactate concentrations and the response to treatment have been shown to have a prognostic value in dogs. Sepsis and shock are common causes of lactic acidosis in the ICU. Considerations in a neurological patient presenting acutely with lactic acidosis include seizures, diabetic ketoacidosis, thiamine deficiency, hypoxia, rhabdomyolysis, hepatorenal failure and poisoning. When lactate levels are profoundly elevated, it is likely that type A and type B acidosis (*Table 14*, next page) are both present. Generalized seizures induce profound muscle activity. In this scenario, oxygen demand may significantly outstrip supply, with resultant widespread muscle hypoxia.

Testing

Many blood gas machines have lactate cartridges available. Lactate can be evaluated from hand-held machines designed for sportsmen and women.

Normal ranges

Lactic acidosis is defined as a pH of <7.35 and a lactate value of >5 mmol/l (45 mg/dl) in human practice. Hyperlactataemia is defined as a lactate value of >2.5 mmol/l (22.5 mg/dl) in dogs and >1.5 mmol/l (13.5 mg/dl) in cats. (*Note:* Severe hyperlactataemia [>20 mmol/l; 180 mg/dl] can resolve with appropriate therapy. Sustained hyperlactataemia, demonstrating a lack of response to treatment, has been associated with a poorer prognosis.)

Monitoring

The frequency of monitoring will be determined by the severity of the clinical disease. During aggressive volume resuscitation, serial lactate measurements may be taken at intervals of 30 minutes or less to evaluate response to therapy.

Treatment

Treatment of lactic acidosis involves identification and treatment of the underlying cause. Oxygen delivery can be optimized through fluid resuscitation and manipulation of cardiac output and arterial oxygen content (see Chapters 2 and 31). The routine use of hyperventilation, sodium bicarbonate or buffers for the treatment of metabolic acidosis is not universally recommended. Reversal of the metabolic acidosis is generally an indication of successful therapy. An increasing base deficit suggests that the therapeutic measures instigated are either inadequate or inappropriate. It is likely that the profound acidosis that is often seen after a generalized seizure does not cause significant physiological compromise *per se* and only requires supportive therapy.

Table 14 Classification and causes of acquired lactic acidosis

TYPE A **Due to tissue hypoxia**	TYPE B **Not due to tissue hypoxia***
• Tissue hypoperfusion	• Sepsis
• Abnormal vascular tone or permeability	• Hepatic failure
• Left ventricular failure	• Renal failure
• Decreased cardiac output	• Hypoglycaemia
• Strenuous muscular exercise	• Diabetes mellitus
• Seizures	• Neoplasia, especially haematological
• Reduced arterial oxygen content	• Cyanide
• Asphyxia	• Ethanol
• Hypoxaemia	• Ethylene glycol
• Carbon monoxide poisoning	• Drugs
• Life-threatening anaemia	• Mitochondrial myopathies
	• Thiamine deficiency

* Non-hypoxic processes affecting the production and elimination of lactate.)



▲ 51 Petechiae on a dog with severe thrombocytopenia.



▲ 52 Epistaxis due to coagulopathy.

Tests of haemostasis

Fundamentals

Animals with defects in haemostasis may present with neurological signs secondary to haemorrhage (e.g. spinal cord or brain parenchymal bleeding secondary to *Angiostrongylus* infection or anticoagulant toxicity). There is also some evidence that traumatic brain injury may itself result in coagulopathy, at least in humans. Defects in platelet numbers or function may be related to the presenting clinical signs (e.g. thrombocytopenia in disseminated intravasular coagulation [DIC]) or may be due to an unrelated disease process (e.g. thrombocytopathia in von Willebrand's disease).

Animals with primary haemostatic disorders may present with petechiae (**51**) or ecchymoses and spontaneous haemorrhage from mucosal surfaces (**52**). This may include hyphaema, haematuria, epistaxis and melaena. However, they commonly present in a similar manner to animals with defects of secondary haemostasis, which are characterized by multiple haematomas,

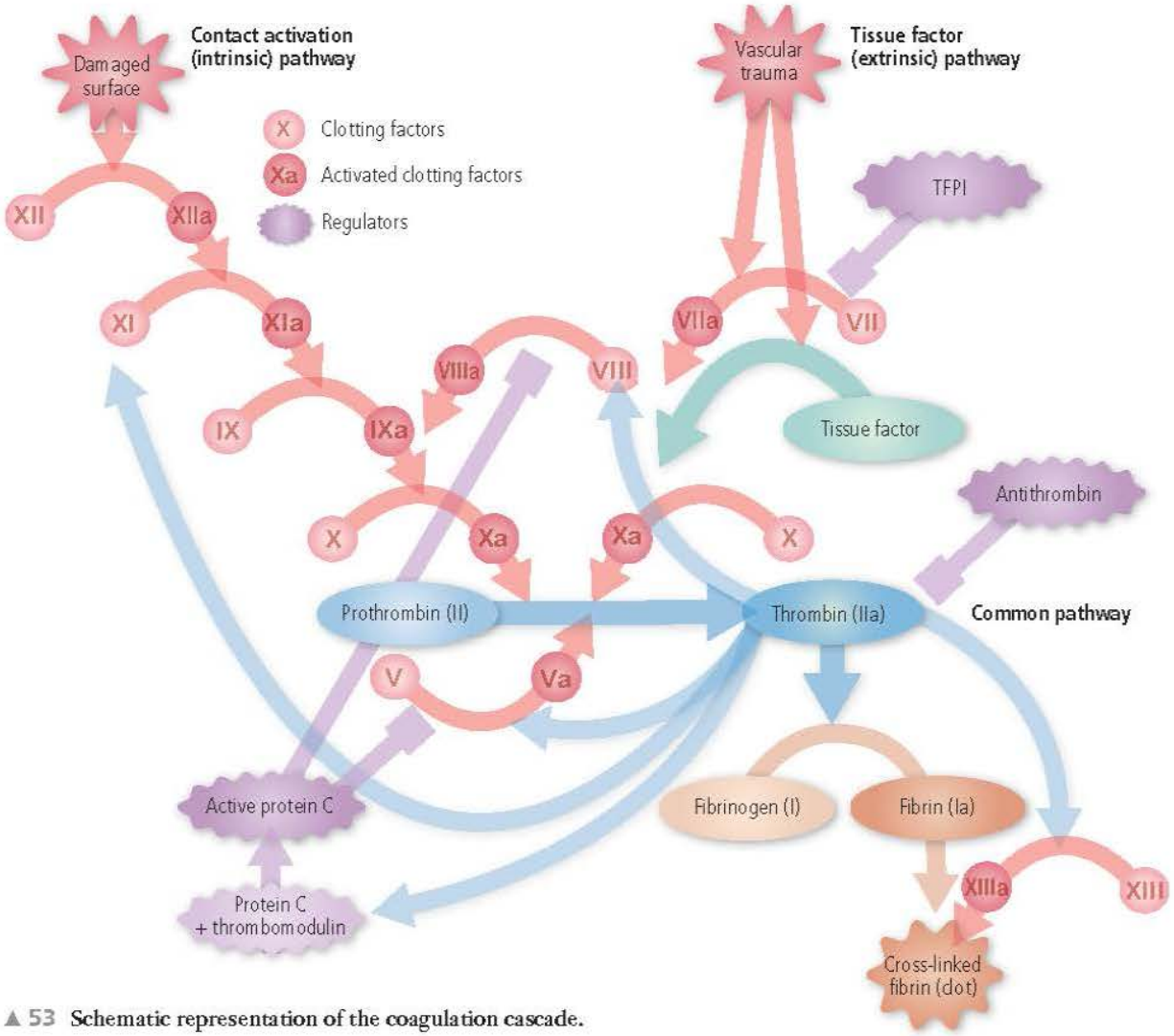
bruises and haemorrhage into joints and body cavities. Acquired disorders (e.g. DIC) do not fit this description because of the multiple abnormalities often present. The assessment of haemostasis should be systematic, based on the clinical and neurological examinations.

Clinical relevance

Thrombocytopenia is a common finding in critically ill patients and results from either lack of platelet production, sequestration, consumption or destruction. It is important to determine the underlying cause of the thrombocytopenia, to determine whether the platelet count is low enough to warrant therapy, and then to act accordingly.

Thrombocytopathia may also be present and may be inherited (e.g. as with von Willebrand's disease) or acquired, either as a result of drug administration or secondary to other disease processes, such as neoplasia.

Coagulopathies result from defects in the coagulation cascade (**53**). They may be either acquired (e.g. DIC, hepatopathies, pharmacologic administration of anticoagulants and vitamin K or rodenticide toxicity) or they may be inherited. The extrinsic (tissue factor) and common pathways of the coagulation cascade can be assessed by determining prothrombin time (PT), and the intrinsic (contact activation) and common pathways by determining the activated partial thromboplastin time (PTT).



▲ **53** **Schematic representation of the coagulation cascade.**

Testing and normal ranges

Platelets should always be counted manually on a smear. Sampling (e.g. clumping) and laboratory artefacts can give erroneous results. Greyhounds tend to have lower numbers of platelets and Cavalier King Charles Spaniels may have macroplatelets. In cats there is an overlap in size between platelets and RBCs, potentially leading to incorrect platelet counts with automated cell counters.

Normal platelet counts range from 200,000–800,000 cells/μl, which equates to 8–15 platelets per ×100 high-power field. Platelet counts below 20,000–50,000 cells/μl may lead to clinical bleeding.

Buccal mucosal bleeding times (BMBTs) should be performed in any animal where a primary haemostatic defect is suspected (**54**). The normal BMBT in the dog is <4.3 minutes and in the cat it is <2.5 minutes. A prolonged BMBT time in a patient with a normal platelet count confirms a thrombocytopathia.

Activated clotting time (ACT) is a screening test for the intrinsic and common pathways of the coagulation cascade. Blood (2 ml) is drawn into a pre-warmed commercial tube that contains diatomaceous earth after discarding the first few drops of blood. The sample is placed in a 37°C (98.6°F) heating bath and inverted every 10 seconds. ACT is the time to first clot formation. ACT is relatively insensitive; it is not abnormal until one factor is less than 10% of normal concentrations or multiple factor deficits are present.



▲ **54** **Buccal mucosal bleeding time testing on a dog with a suspected primary haemostatic defect. The upper lip of the dog is folded back and held in place with a gauze bandage. This causes moderate engorgement of the mucosal surface. A bleeding device creates a small incision in the buccal mucosa. A timer is started and at 15 seconds a filter paper is placed 1–3 mm below the incision, without dislodging the clot, to stop the blood flow. The timer is stopped when bleeding ceases.**

Portable machines are available for the assessment of PT and activated PTT. It is important that the correct methodology is followed to prevent erroneous results. Normal values are supplied by the manufacturer. It is an excellent screening test, but false positives do occur in both the PT and the activated PTT tests and some defects of the extrinsic pathway will not be detected. It is prudent to validate all abnormal results by conventional methodology.

D-dimers are fibrin split products that indicate the activation of thrombin and plasmin. Several bedside tests have been developed involving various technologies. They are reasonably sensitive, but not specific for DIC.

Monitoring and treatment

Treatment of coagulopathies is based on the appropriate administration of canine or feline blood products including fresh frozen plasma, cryoprecipitate and platelet-rich plasma (not available globally). Further details of fluid therapy can be found in Chapter 31.

Ammonia

Ammonia is elevated in animals with significant liver disease or portosystemic shunts. While less sensitive than bile acids for the detection of hepatic dysfunction, the presence of an elevated circulating ammonia concentration warrants immediate treatment. Hyperammonaemia may contribute to the clinical signs of hepatic encephalopathy, and therefore appropriate treatment can produce a marked clinical improvement. (See Chapter 27 for further details on management of hepatic encephalopathy.)

Temperature regulation

Fundamentals

Thermoregulation is controlled mainly by the hypothalamus. Such homeostatic control is separate from the conscious sensation of temperature. The overall integrated responses that maintain normothermia despite changes in external environment and physical workload are complex and are integrated by the hypothalamus. When body temperature increases, neurons in the hypothalamus turn on mechanisms for heat dissipation that include sweating and dilation of blood vessels in the skin. When body temperature decreases, neurons in the hypothalamus are responsible for heat production through shivering, vasoconstriction in the skin and piloerection. Therefore, lesions in the hypothalamus can result in hyperthermia or hypothermia when the environmental temperature is low. The hypothalamus also contains the 'biological clock', which regulates certain body functions that vary at different times of the day (e.g. body temperature, hormone secretion, hunger) or those that vary over a period of many days.

Clinical relevance

Severe traumatic brain injury can result in hyperthermia secondary to hypothalamic damage. (*Note:* This damage may have other effects, such as blocking the production of ADH, resulting in DI.) Other lesions that affect the hypothalamus may potentially affect thermoregulation. Hyperthermia can also result when the underlying cause for the neurological presentation is heatstroke. This is a life-threatening situation and must be managed appropriately and aggressively (see Chapter 27).

More commonly, obtunded and immobile animals present with a decreased rectal (and core) body temperature. Clinicians should be aware that moderate to severe hypothermia can influence the findings of the neurological examination. There is some evidence that patients that present with hypothermia secondary to disease, trauma, surgery or drug-induced alterations in heat production and thermoregulation have more severe clinical signs when less severely hypothermic than those that are accidentally hypothermic through exposure to low environmental temperature alone.

Testing

Oesophageal temperature is often considered to approximate core temperature. However, this cannot be obtained in conscious or sedated patients, therefore rectal temperature is most commonly used as a surrogate. (*Note:* The introduction of a thermometer into the rectum can cause straining and a rise in ICP.) Oesophageal probes inserted into inadequately anaesthetized patients can cause gagging and coughing, with a similar outcome.

Normal ranges

There is some diurnal variation in body temperature. The normal ranges for daytime body temperatures are: dog, 37.5–39.2°C (99.5–102.5°F); cat, 37.8–39.5°C (100–103.1°F).

Monitoring

Hypothermic animals should have their rectal temperature (if conscious) or core temperature (if intubated) measured at least every 30 minutes to ensure that they are responding appropriately to treatment. Where an animal is normothermic but considered to be at risk from becoming pyrexic (e.g. through sepsis), it is prudent to measure rectal temperature every 4–6 hours.

Treatment

Hyperthermia increases cerebral metabolic oxygen demand, may cause cerebrovasodilation and should generally be avoided. Severe hyperthermia can manifest as neurological abnormalities. Active cooling must be undertaken if the temperature is significantly >39.5°C (103.1°F). This can be achieved by dousing the fur with tepid water and blowing air across the patient. Additional measures, such as cool water enemas or peritoneal lavage (10–20 ml/kg room temperature sterile saline), may be required, although experimental studies suggest that evaporative cooling may be as effective as peritoneal lavage.

Aggressive cooling will be required where animals present with neurological signs secondary to heat stroke. Cooling may also be required in patients with seizure-induced hyperthermia. Care must be taken to avoid rebound hypothermia in such patients. Some guidelines suggest that cooling should be stopped when the body temperature reaches 39.5°C (103.1°F).

Animals that present with hypothermia should be actively warmed, ideally with circulating warm air blankets or in an incubator. Warm fluids may also be administered. Heat pads, 'hot hands' or hot water bottles and warmed bedding may also be utilized (**55**). Extreme care should be taken to avoid contact burns from direct heat sources. (*Note:* Examination and nursing procedures will predispose to further decreases in body temperature and care should be taken to minimize further heat loss.) It is prudent to avoid sedation or anaesthesia until the body temperature is within normal limits.

Induced hypothermia for the treatment of refractory intracranial hypertension remains a controversial topic in human neurointensive care. The only potential indication in veterinary intensive care appears to be in prolonged cardio–pulmonary–cerebral resuscitation (CPCR). There is some evidence that mild or moderate hypothermia during prolonged CPCR in dogs preserves the viability of extracerebral organs and improves outcome. Therefore, there are currently no indications for permissive hypothermia in critically ill veterinary neurology patients. Most patients present with mild hypothermia and require active warming.

COMMON METABOLIC ABERRATIONS IN SPECIFIC NEUROLOGICAL PRESENTATIONS

While every case must be approached on an individual basis, particular metabolic aberrations are seen in certain neurological presentations and may only be diagnosed following appropriate testing. They do not occur in all patients with a specific presentation, but should be considered during clinical evaluation. Equally, other findings may also be present that are not listed in *Table 15*.



▲ **55** Forced warm air heating being used to maintain normothermia in a critically ill patient.

Table 15 **Common metabolic aberrations in specific neurological presentations**

PRESENTATION	EVALUATION METHOD	FINDINGS/AETIOLOGY
Traumatic brain injury	CBC evaluation	• Anaemia – haemorrhage • Haemoconcentration – hypovolaemia
	Biochemical evaluation	• Pre-renal azotaemia – hypovolaemia • Hyperglycaemia – catecholamine release • Hyponatraemia – SIADH • Increased TP – haemoconcentration • Decreased TP – haemorrhage
	Urinalysis	• Often increased USG and decreased urine output – hypovolaemia • SIADH leads to urine sodium >20 mmol/l and osmolality >150 mmol/l
	Osmolality	• SIADH leads to serum osmolality <280 mmol/l
	Blood gas analysis	• Evidence of hypoperfusion: metabolic acidosis • Decreased pH • Decreased HCO_3^- • Increased base deficit • Increased lactate • Changes in $PaCO_2$, especially if brainstem involved • Changes in PaO_2 – pneumothorax, pulmonary contusions, atelectasis and aspiration pneumonia
	Coagulation evaluation	• Purported increased PT/aPTT
	Endocrine analysis	• Acute adrenal failure (hypoadrenocorticism), central hypothyroidism, SIADH, diabetes insipidus. (*Note*: Do not present acutely at time of injury)
	Temperature	• Abnormalities possible
Cerebrovascular accident	Biochemical evaluation	• Evidence of underlying systemic disease (e.g. Cushing's syndrome, hypothyroidism) • Hyperglycaemia, hyponatraemia – SIADH
	Urinalysis	• SIADH leads to urine sodium >20 mmol/l and serum osmolality <280 mmol/l
	Coagulation evaluation	• Increased PT/aPTT
	Endocrine analysis	• Based on minimum database
	Temperature	• Abnormalities possible
Seizure	Biochemical evaluation	• Elevated CK, AST, ALP and ALT • Hypoglycaemia (uncommon) • Hyperglycaemia • Hyperkalaemia

(Continued)

Table 15 **Common metabolic aberrations in specific neurological presentations** (*continued*)

PRESENTATION	EVALUATION METHOD	FINDINGS/AETIOLOGY
Seizure	Urinalysis	• Myoglobinuria reported to lead to renal failure
	Blood gas analysis	• Lactic acidosis – muscular contractions • Increased $PaCO_2$ – increased CO_2 production and hypoventilation. (*Note*: May be exacerbated by drug administration) • Iatrogenic alkalaemia may reduce the seizure threshold • Changes in PaO_2 – atelectasis and aspiration pneumonia
	Coagulation evaluation	• Increased PT/aPTT promoted by hyperthermia • DIC – extremely rare
	Temperature	• Hyperthermia secondary to seizure activity
Intracranial mass/lesions	CBC evaluation	• Anaemia of chronic disease (inconsistent) • Haemoconcentration – hypovolaemia
	Biochemical evaluation	• Evidence of co-existing disease or systemic disease • Pre-renal azotaemia – hypovolaemia • Increased TP – haemoconcentration • Decreased TP – haemorrhage • Multiple electrolyte abnormalities possible depending on anatomical location
	Urinalysis	• Often increased USG and decreased urine output – hypovolaemia
	Osmolality	• Consider electrolyte changes in interpretation
	Blood gas analysis	• Evidence of hypoperfusion: metabolic acidosis • Decreased pH • Decreased HCO_3^- • Increased base deficit • Increased lactate • Changes in $PaCO_2$, especially if brainstem involved • Changes in PaO_2 – atelectasis and aspiration pneumonia
Pituitary tumour	CBC evaluation	• May be consistent with endocrinopathy
	Biochemical evaluation	• Look for evidence of endocrinopathy (e.g. hyponatraemia – SIADH, hypoadrenocorticism; hyperkalaemia – hypoadrenocorticism; hypochloridaemia – secondary to SIADH) • Hypernatraemia, hyperchloridaemia and hypokalaemia reported • Increased urea – precludes SIADH, present in hypoadrenocorticism • (*Note*: Multiple electrolyte abnormalities reported)

(Continued)

Table 15 **Common metabolic aberrations in specific neurological presentations** (*continued*)

PRESENTATION	EVALUATION METHOD	FINDINGS/AETIOLOGY
	Urinalysis	• Increased USG and decreased urine output – hypovolaemia • Decreased USG – diabetes insipidus/ Cushing's syndrome/hypoadrenocorticism • SIADH leads to urine sodium >20 mmol/l and osmolality >150 mmol/l
	Osmolality	• SIADH leads to serum osmolality <280 mmol/l
	Endocrine analysis	• Cushing's syndrome, central hypothyroidism, SIADH, diabetes insipidus, hypoadrenocorticism
	Temperature	• Abnormality possible
Neuromuscular diseases	CBC evaluation	• Evidence of primary systemic disease
	Biochemical evaluation	• Elevated serum cardiac troponin-I • Elevated CK and AST • Evidence of endocrine or electrolyte abnormalities in aetiology • Hypokalaemia due to lack of oral intake
	Urinalysis	• Myoglobinuria
	Blood gas analysis	• Increased $PaCO_2$ – hypoventilation • Changes in PaO_2 – atelectasis and aspiration pneumonia
Tetanus	CBC examination	• Neutrophilic leukocytosis
	Biochemical evaluation	• Elevated CK and AST • Hypokalaemia due to lack of oral intake
	Urinalysis	• Watch for urinary retention
	Blood gas analysis	• Increased $PaCO_2$ – hypoventilation exacerbated by sedatives • Changes in PaO_2 – atelectasis and aspiration pneumonia, nurse on an incline
Exogenous acute spinal cord injury	CBC evaluation	• Anaemia – haemorrhage
	Evaluation method	• Haemoconcentration – hypovolaemia
	Biochemical evaluation	• Evidence of co-existing disease • Pre-renal azotaemia – hypovolaemia • Increased TP – haemoconcentration • Decreased TP – haemorrhage • Electrolyte abnormalities – urinary tract rupture
	Urinalysis	• Often increased USG and decreased urine output – hypovolaemia

(Continued)

Table 15 **Common metabolic aberrations in specific neurological presentations** (*continued*)

PRESENTATION	EVALUATION METHOD	FINDINGS/AETIOLOGY
	Blood gas analysis	• Evidence of hypoperfusion: metabolic acidosis • Decreased pH • Decreased HCO_3^- • Increased base deficit • Increased lactate • Changes in $PaCO_2$, especially if high cervical lesion • Changes in PaO_2 – pneumothorax, pulmonary contusions, atelectasis and aspiration pneumonia

SIADH = syndrome of inappriate antidiuretic hormone secretion; USG = urine specific gravity; PT = prothrombin time; aPTT = activated partial thromboplastin time; CK = creatine kinase; AST = aspartate aminotransferase; ALP = alkaline phosphatase; ALT = alanine aminotransferase; DIC = disseminated intravascular coagulation; TP= total protein.

IMAGING OF NEUROLOGICAL EMERGENCIES

Fraser McConnell

INTRODUCTION

Diagnostic imaging is important in the characterization and identification of gross structural abnormalities affecting the nervous system. All imaging studies in the neurological patient should be preceded by clinical assessment aimed at ruling out non-neurological causes of signs (e.g. bilateral cruciate ligament rupture or systemic disease), determining the lesion localization within the nervous system and identifying possible concurrent injuries. The role of imaging is not to determine if the clinical signs are neurological in origin. As with anatomical imaging elsewhere in the body, functional disorders and diseases that do not result in a gross structural change in an organ may not be visible on images. Such imaging is only useful if interpreted along with the patient's signalment and history and with the information provided by a comprehensive neurological examination.

Which imaging modality to use?

The choice of imaging modality depends on the neurolocalization and what is available (**56**, page 85). Advanced neuroimaging is expensive and interpretation is dependent on correlation of the neurological examination with the imaging findings. Magnetic resonance imaging (MRI) or computed tomography (CT) should not be used as substitutes for a thorough neurological evaluation. MRI requires general anaesthesia and imaging may need to be delayed until the animal's condition is stable. If the neurological examination indicates a central lesion, advanced imaging will be required to rule in/out a gross structural lesion. Other than in cases of known or suspected trauma, MRI is preferred to CT due to its excellent soft-tissue contrast. In the majority of cases of intracranial disease, radiography is of limited or no value. The advantages and disadvantages of the different imaging modalities are shown in *Table 16*, next page.

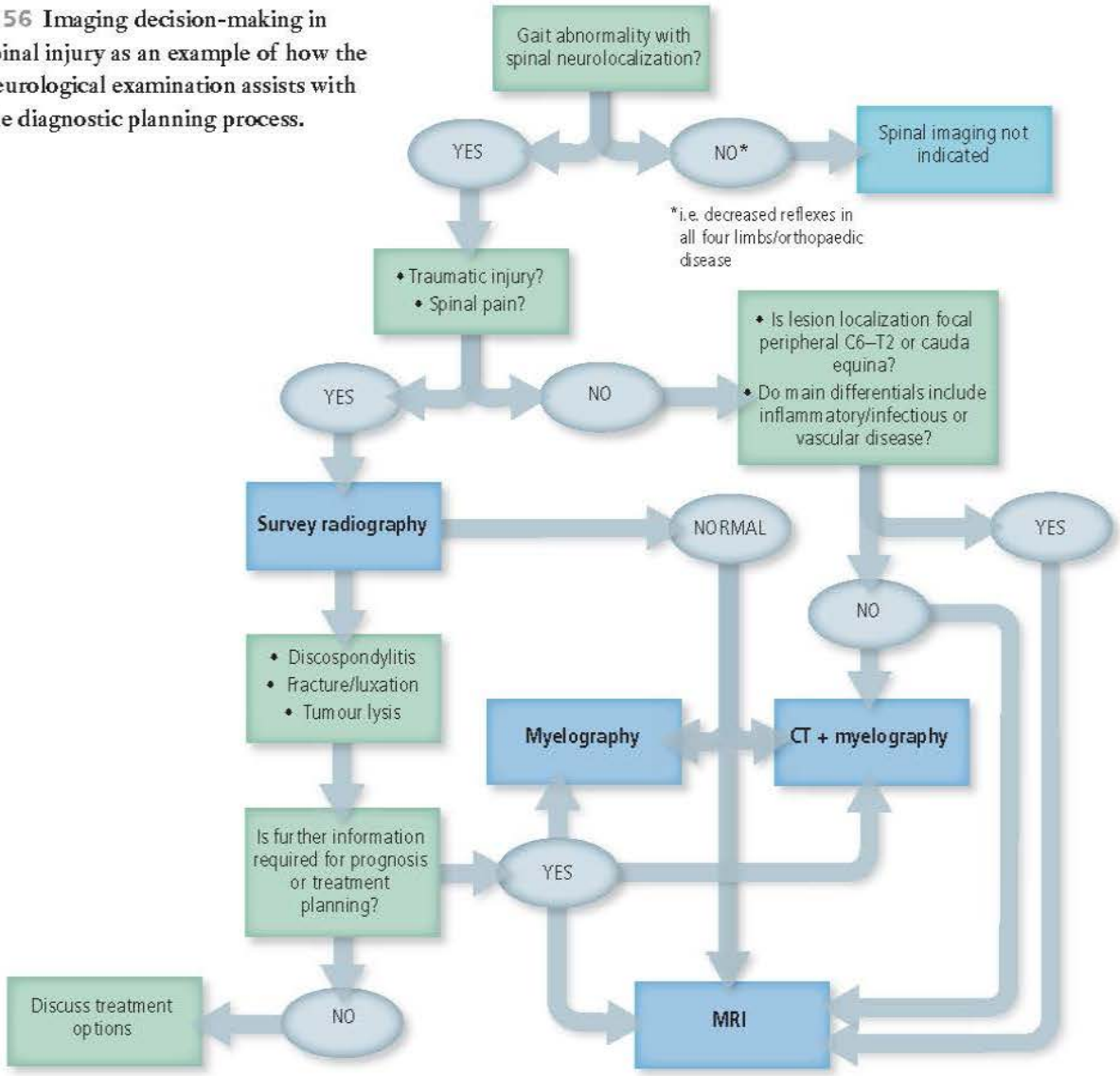
Patient handling

The majority of imaging studies will require sedation or general anaesthesia (GA), which may exacerbate neurological disease; the risk/benefits of anaesthesia and imaging need to be considered in light of the clinical and neurological examination. (Further information on anaesthesia for these procedures can be found in Chapter 29.) With neurological disease caused by high-impact trauma or spinal instability, care needs to be taken when moving and positioning the animal for imaging studies. Manipulating animals with unstable spinal lesions for any imaging modality may exacerbate spinal cord injuries. In cases where spinal trauma is suspected it is essential that the animal is handled without torsion/rotation or excessive flexion/extension of the spine. High-quality radiographs are required to diagnose many spinal conditions and this requires the use of GA or sedation. Sedation/GA, however, results in muscle relaxation and can reduce the protective 'splinting action' of the paraspinal muscles, thus potentially exacerbating spinal fractures/luxations. In cases of known or suspected spinal fractures or high-impact trauma, survey radiographs should be taken with the animal conscious, and these may be adequate to reveal gross fractures or luxations. If survey radiographs fail to identify lesions, better quality radiographs can be taken once the animal is anaesthetized. (*Note:* In cases of spinal trauma, assume that there is an unstable fracture until proven otherwise.)

Table 16 **Comparison of imaging modalities**

MODALITY	ADVANTAGES	DISADVANTAGES
Radiography	Cheap and readily available. Useful for diagnosis of spinal fractures/luxation, bony congenital malformations, discospondylitis and neoplasia if involving bone. Dynamic studies possible. Chest and abdominal imaging useful in investigating systemic causes of neurological disease	Technique critical for subtle lesions. May be time consuming. No information on brain or spinal cord without use of contrast medium. Very limited utility for brain disease. Limited information about paraspinal soft tissues. Most cases need GA/sedation unless suspect fracture/instability
Myelography	Readily available. Good for overview of spine as can image entire spinal cord relatively quickly. Accurate and sensitive for identifying sites of spinal cord compression. Dynamic studies possible	Invasive and requires use of ionizing radiation. GA required. May be difficult to perform in obese dogs. Technique critical to obtain fully diagnostic study. Does not provide information on brain or peripheral nerves. Provides limited information compared with MRI/CT for intramedullary or intradural lesions
Computed tomography	Quick to perform (especially multislice CT units). Excellent bone imaging and easy to perform 3-D reconstructions. Useful for evaluation of complex bony malformations and fractures. Modality of choice for assessing bony lesions. Acute disc extrusions can be identified without the need for contrast. Much better soft-tissue contrast than radiography and cross-sectional imaging means lack of superimposition. Can be performed following insertion of surgical implants and where metallic fragments are present within the body. Dynamic studies possible	Requires GA/sedation. Expensive and limited availability. Evaluation of spinal cord often requires CT myelogram. Older machines may give poor reconstructions in oblique planes. Artefacts may prevent evaluation of brainstem/caudal fossa lesions. Poor soft-tissue contrast compared with MRI
Magnetic resonance imaging	Excellent soft-tissue contrast and ability to obtain images in any plane. Does not use ionizing radiation. Modality of choice for investigation of brain, soft tissues, spinal cord and peripheral nerve lesions. Capable of detecting haemorrhage	Expensive and time consuming. Image quality variable (user and equipment dependent). May be difficult adequately to image very large dogs or small cats/dogs. Cannot be used if mobile metal fragments within body or surgical implants in area of interest. Limited dynamic studies
Ultrasound	Widely available, cheap and does not require GA/sedation. Allows guided biopsy/aspiration. May be used to identify peripheral nerve masses/lesions. Allows aspiration of disc material in cases of discospondylitis. If open fontanelle is present, may be used to diagnose hydrocephalus	In most animals limited use due to inability of ultrasound to penetrate thick bones of the skull and spinal column

Animals with spinal trauma can be restrained on a rigid board (e.g. plywood or non-metallic stretcher [**57**]) for radiography. Radiographs obtained through a board will have reduced image quality, but should show large displaced fractures/luxations. Similar care should be taken when positioning patients for advanced imaging. Small dogs and cats can be positioned in a radiographic positioning trough, which will support the spine. For larger dogs, sufficient personnel should be present to ensure that all parts of the spine and head are supported when rotating the patient.



▶ 56 **Imaging decision-making in spinal injury as an example of how the neurological examination assists with the diagnostic planning process.**



◀ 57 **Animals with potential spinal injuries should be handled carefully when being moved for imaging. The use of a stretcher, as in this case, allows the animal to be moved with reduced risk of exacerbating any potential injury. It is possible to radiograph animals through non-metallic stretchers.**

SURVEY RADIOGRAPHY

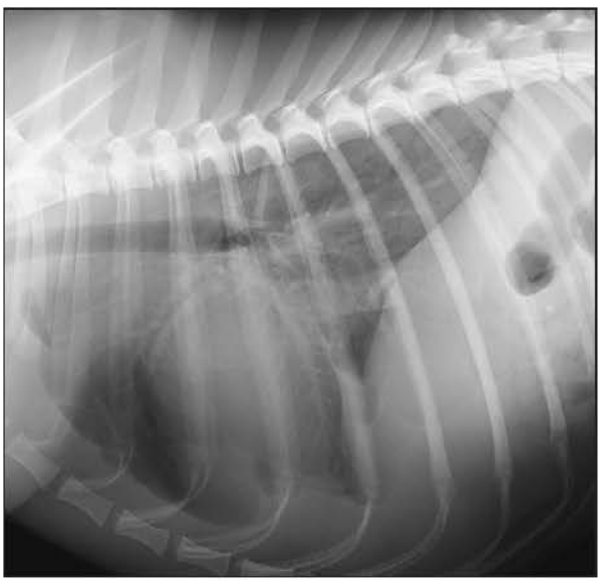
Survey radiographs of the thorax are indicated in all animals that have been involved in a road traffic accident (RTA) or suffered other high-impact trauma. There is a high incidence of concurrent thoracic injury associated with long bone and spinal fractures (21% in one study) (**58**). Such injuries may preclude GA for advanced imaging or other investigations until the animal has been stabilized. If there are clinical signs of respiratory disease, thoracic radiographs should be obtained. Thoracic radiographs may identify thoracic pathology secondary to intracranial disease or neuromuscular/peripheral nerve diseases. For example:

- Megaoesophagus.
- Aspiration pneumonia.
- Non-cardiogenic pulmonary oedema (uncommon) (**59**).
- Lung metastases from a primary brain tumour (rare).

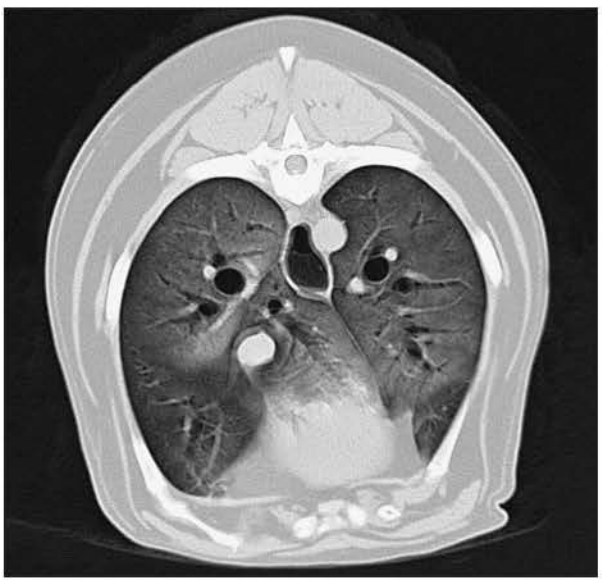
Survey radiography of the spine and cranium provides information largely limited to the osseous component of the skeleton; however, without the use of contrast (myelography) it provides minimal information on the spinal cord (**60, 61**). Nonetheless, plain radiographs are quick to obtain and relatively cheap, but in many cases of neurological emergency have a low diagnostic yield. There is often a poor correlation between radiographic abnormalities and neurological status, and fractures are often missed.

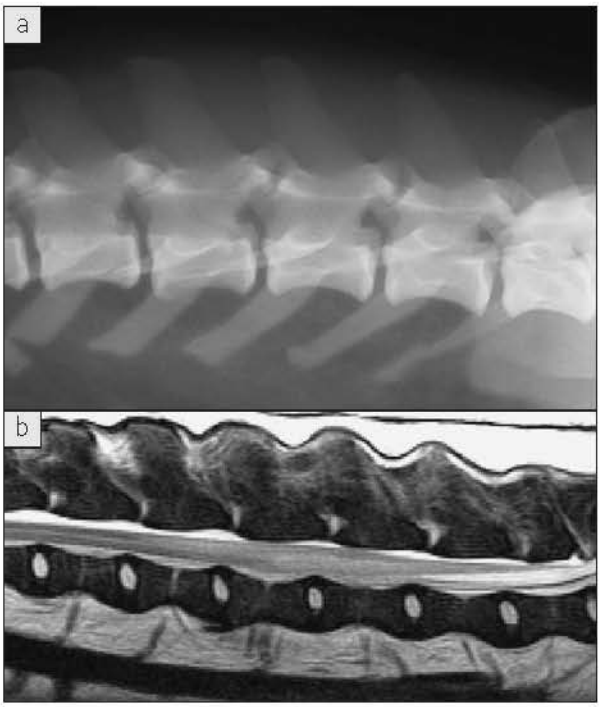
Radiography has a very low diagnostic yield for the diagnosis of intracranial pathology and survey radiographs are not usually indicated unless there is external swelling or a known history of severe head trauma. Even in cases of skull fractures, radiography will not provide information on the severity of the brain injury and many

▼ **58** **Lateral thoracic radiograph of an 18-month-old Whippet with acute-onset paraplegia following a presumed traumatic incident. The radiograph shows the presence of pleural fluid. There is a high incidence of thoracic injuries associated with pelvic and spinal fractures. Non-neurological injuries should be assessed and identified prior to general anaesthesia for imaging.**

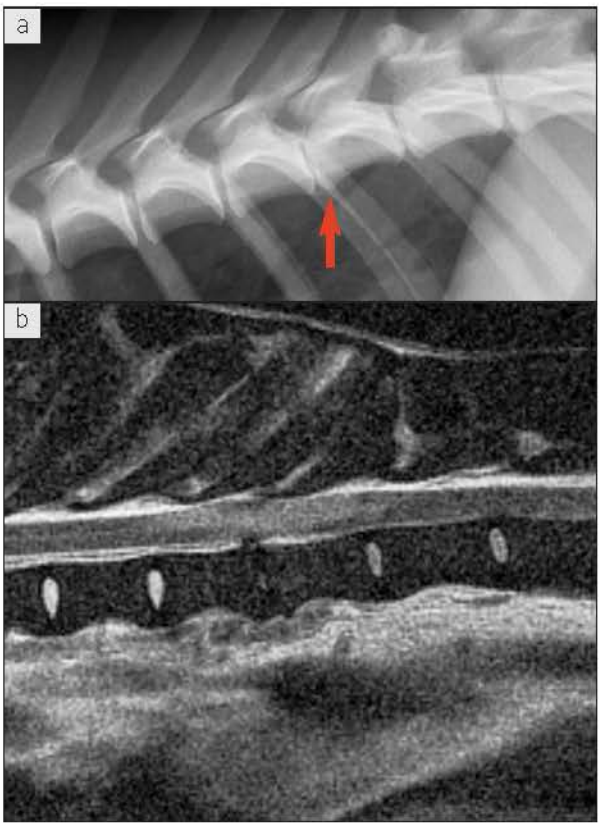


▼ **59** **CT image of a Flat-coated Retriever with non-cardiogenic pulmonary oedema (in this case secondary to upper airway obstruction). Similar changes may occur secondary to intracranial disease (seizures, increased intracranial pressure). Neurogenic non-cardiogenic pulmonary oedema is thought to occur secondary to massive release of catecholamines resulting in peripheral vasoconstriction and myocardial ischaemia.**

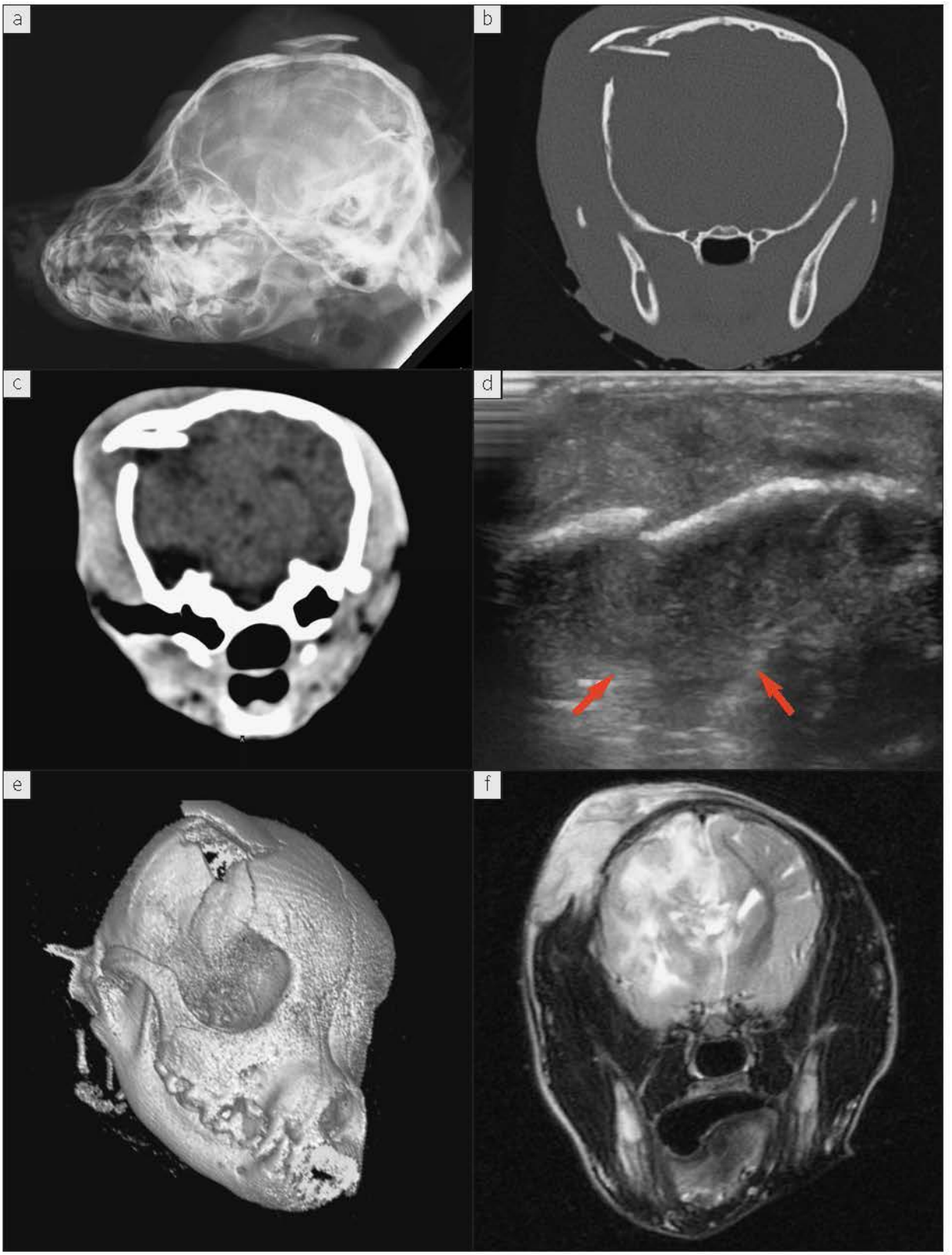




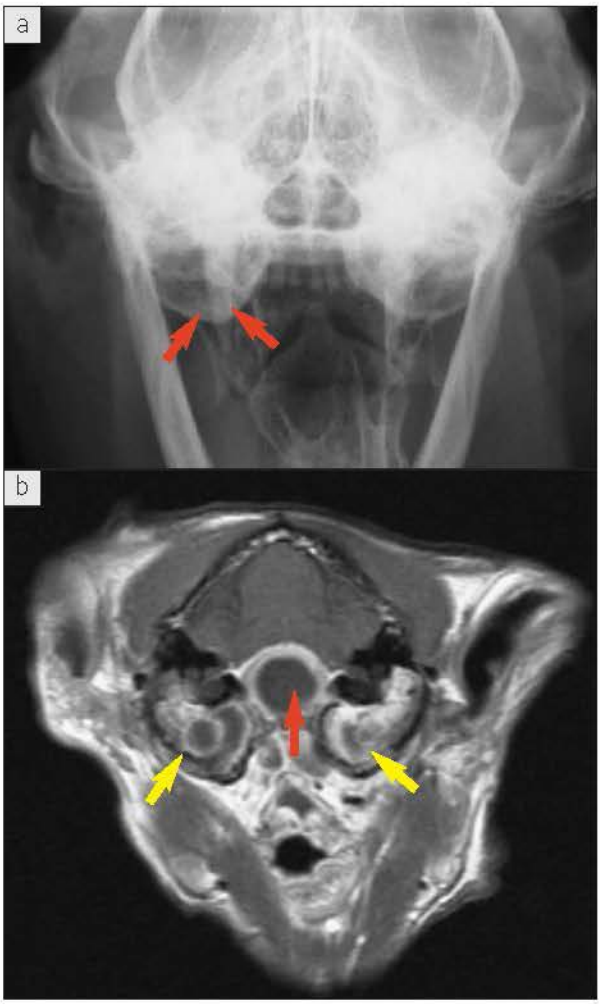
▶ 60 Lateral radiograph (a) and sagittal T2-weighted MR image (b) of the lumbar spine of a 2-year-old male Staffordshire Bull Terrier following trauma (hit by car). The radiograph is within normal limits, but the MR image shows severe swelling and diffuse increased signal within the spinal cord consistent with contusion/oedema. Radiographs give information about the osseous components of the spine and limited or no information on the soft tissues. The severity and extent of the spinal cord changes have some correlation with prognosis, with more extensive cord changes having a poorer prognosis. In this case the dog recovered some hindlimb function, but was unable to urinate.



▶ 61 Lateral radiograph (a) and sagittal T2-weighted MR image (b) of the thoracic spine of an 18-month-old Whippet with a traumatic intervertebral disc extrusion (same dog as 58). The radiograph shows subtle narrowing of the disc space at T9/10 (arrow) and ventral subluxation of T10. The severity of the spinal cord injury cannot be determined from the radiograph. The MR image shows extensive spinal cord changes including swelling and increased signal consistent with contusion/concussive injury.


a
b
c
d
e
f

◀ **62** Lateral oblique radiograph (a), CT image with a bone window and algorithm (b), CT image with a soft-tissue window and algorithm (c), ultrasonographic image (d) and CT 3-D reconstruction (e) of a Yorkshire Terrier with a skull fracture secondary to a dog bite injury. The skull radiograph shows the large fragment that lies superficial to the skull defect, but the depressed fragment that compresses the brain is not seen. The CT study allowed accurate assessment of the fracture and localization of the fracture and the presence of hypoattenuating fluid/tissue adjacent to the depressed fragment, which probably represents oedema/contusion. The 3-D reconstruction adds no further information in this case, but can aid interpretation and surgical planning of complex fractures or malformation. The ultrasound image shows the presence of echogenic fluid (arrows) adjacent to the fractures, consistent with haemorrhage or seroma. (f) Transverse T2-weighted MR image of a different dog with a penetrating injury of the brain due to a dog bite. Compared with (b) and (c) the MR image gives much more information on the extent and nature of the brain injury and still allows accurate assessment of the fractures.



▶ **63** Rostrocaudal open mouth radiograph (a) and transverse T1-weighted MR image post contrast at the level of the tympanic bullae (b) of a cat with otitis media. The radiograph shows the typical appearance of chronic otitis media, with increased opacity within the bullae and thickening of the bullae walls (arrows). The MR image, in addition to the bulla pathology (yellow arrows), shows extension of the infection into the caudal fossa, with a large abscess/fluid accumulation around the brainstem (red arrow). The brainstem is displaced dorsally and compressed by the abscess.

skull fractures may be missed (**62**). Depressed fractures or swellings will only be visible if the x-ray beam is tangential to the lesion. A specific lesion-orientated oblique view may be required. This is obtained by angling the x-ray beam so that it skylines the swelling or depression.

Skull radiographs can be used in the investigation of peripheral vestibular syndromes and facial nerve paresis due to otitis media/interna, but have limited value in the investigation of most CN or peripheral nerve lesions. Survey radiography to assess the bullae in cases of peripheral vestibular disease involves a rostrocaudal open mouth oblique or lateral obliques and a dorsoventral (DV) view. The sensitivity of radiography for the diagnosis of otitis media compared with CT was only 85% in one study, with a specificity of 68%. Bullae radiographs may be difficult to interpret in large dogs due to large amounts of overlying soft tissue, and radiographs provide no information about the intracranial extension of otitis media (**63**). Soft-tissue/fluid opacity within the bullae may also be non-significant, as primary secretory otitis is a common, apparently incidental, finding in brachycephalic dogs.

Radiographic technique

Spinal radiography requires high-quality radiographs, as many lesions are subtle and may be missed if the radiographs are suboptimal. For small dogs and cats, a tabletop technique with a high-resolution film–screen combination and small focal spot should be used to maximize image detail. For larger dogs (>10 cm thickness) and obese animals, a grid and bucky should be used.

Orthogonal views (lateral and ventrodorsal [VD]/DV) should be obtained in all cases (**64**) and specific oblique projections may be required to visualize the dens and intervertebral foramina of the cervical spine.

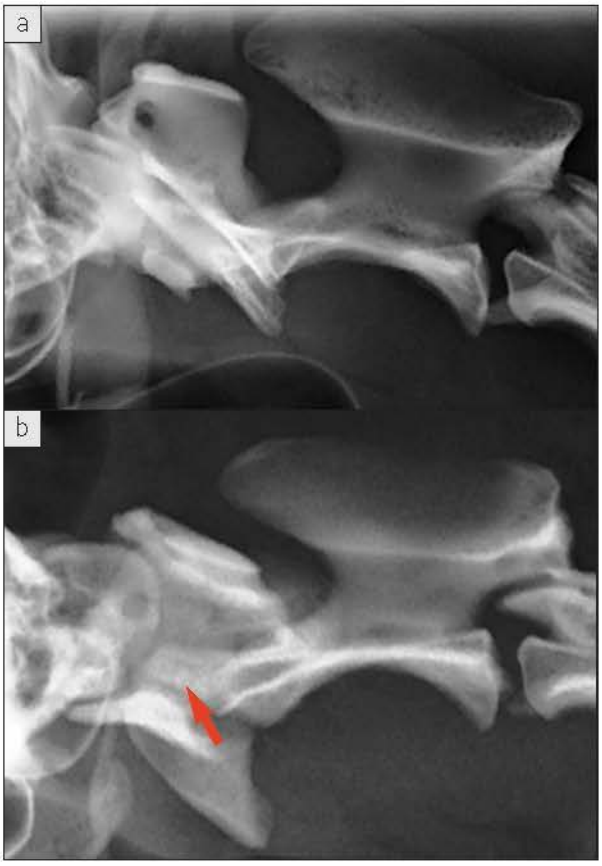
In cases of suspected spinal fracture, a horizontal beam can be used to obtain a VD or DV projection and this is preferable to trying to rotate the animal. The animal is kept in lateral recumbency and the x-ray tube head is rotated through 90° with the x-ray cassette placed dorsal to the spine (**65**). With some digital radiography systems, the x-ray detector is built into the x-ray table, in which case horizontal beam radiography may not be possible. If the animal needs to be moved, there should be enough assistants to stabilize the spine and head to prevent axial rotation while the animal is rotated.



▶ **64** Lateral (a) and ventrodorsal (b) radiographs of the lumbar spine of a cat with a fracture-luxation at L4/5. The degree of overriding is underestimated on the lateral radiograph, although the fracture is clearly visible with shortening of the vertebral body of L4 and a step in the ventral surface of the vertebral body. The ventrodorsal projection shows an obvious displacement of the L4 vertebra to the right and the vertebral fracture is more clearly seen. Orthogonal projections are required to assess accurately the alignment of the vertebral canal. Note the difference in appearance of the spinous processes cranial and caudal to the fracture. This is due to torsion of the caudal part of the spine relative to the cranial segment. The vertebral canal is reduced in width by approximately 30% on the radiographs, but the degree of spinal cord compression and severity of spinal cord pathology cannot be determined without advanced imaging or myelography.



▲ **65** The use of a horizontal x-ray beam allows a ventrodorsal radiograph to be taken with the animal lying in lateral recumbency. An orthogonal view can be obtained without moving the animal. Care needs to be taken with radiation safety when using a horizontal beam.



▶ **66** Lateral (a) and left 30° ventral-right dorsal oblique (lateral oblique) (b) radiographs of C1/C2. On the standard lateral projection the dens is overlying and obscured by the wings of C1. The lateral oblique projection allows clear visualization of the dens (arrow) without the need to flex the neck.

Assessment of the dens of C2 is important in cases of cervical trauma and suspected atlantoaxial (AA) instability. The rostrocaudal oblique view to assess the dens is contraindicated in cases where AA instability is suspected, as the extreme flexion required for this view will cause spinal cord compression. A lateral oblique view of the cervical spine allows assessment of the dens without requiring neck flexion (**66**). The animal is positioned as for a lateral cervical spinal radiograph and rotated dorsally by 20–30° (by placing small foam wedges under the mandible and sternum). (*Note:* Stressed views may demonstrate an instability not visible on radiographs taken with the spine in a neutral position, but they may exacerbate spinal cord injury.)

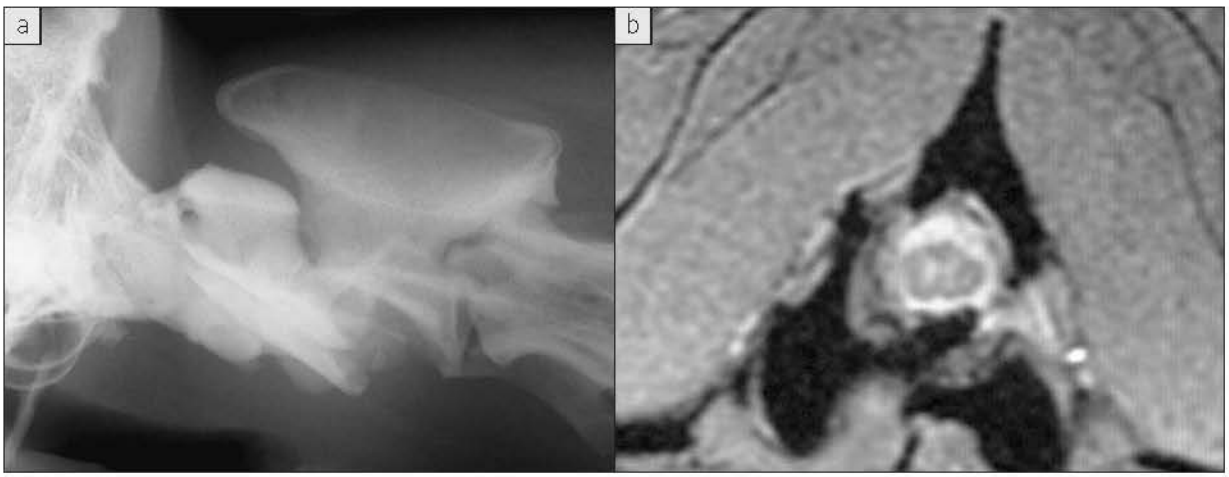
Lateral oblique views of the cervical spine allow assessment of the intervertebral foramina, which are not visible on a lateral projection. Positioning is as for a VD projection of the cervical spine, with the animal then tilted laterally by 45°.

Assessment of spinal radiographs

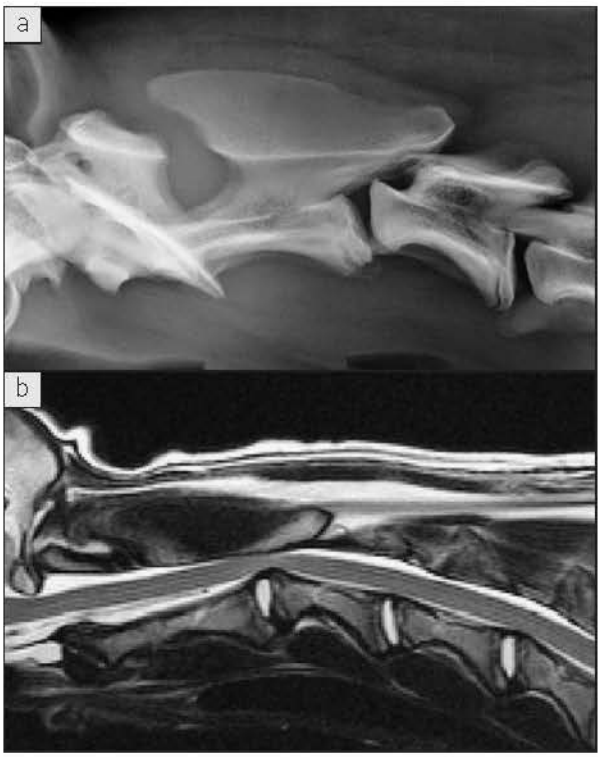
A systematic approach to the assessment of spinal radiographs is important and the following should be critically evaluated:

- The vertebral canal as a whole:
  - Check for alterations in alignment on both projections (**64**).
  - Look for presence of any steps, which indicates luxation. This is most easily performed by critical evaluation of the alignment of the dorsal part of the vertebral bodies and the dorsal laminae on the lateral projections.
  - Look at alignment of the spinous processes, pedicles and lateral margins of the vertebral bodies on the VD projection.

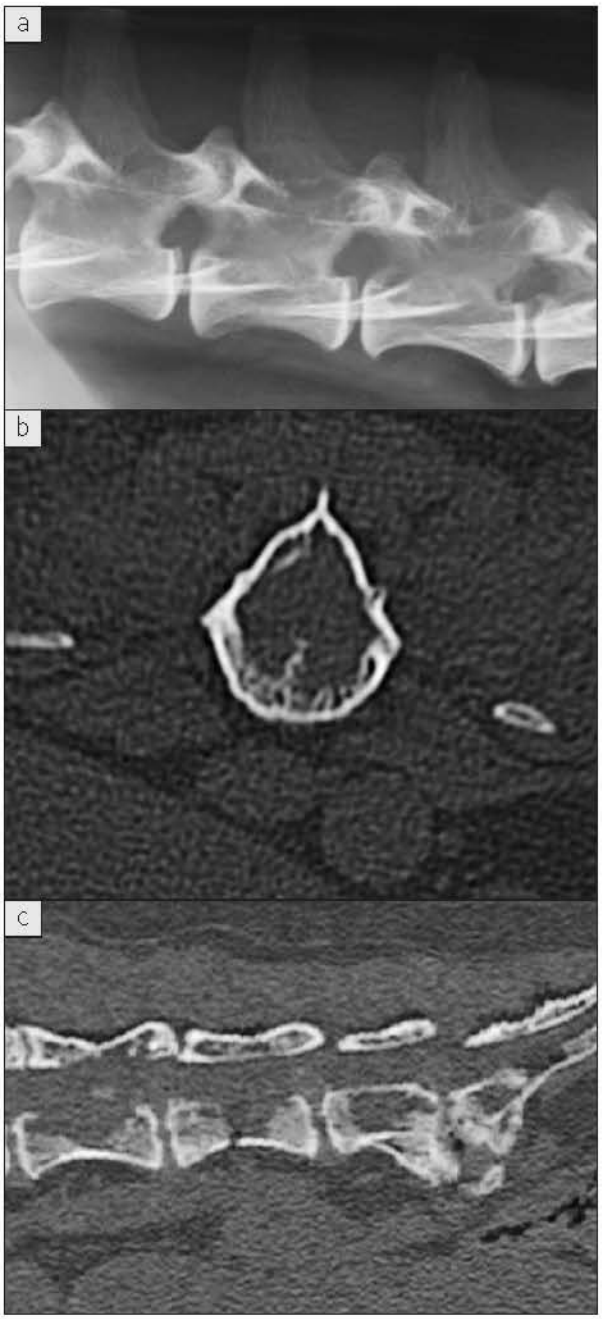
- The width of the vertebral canal:
  - Look for bone extending into the vertebral canal (**67**, **68**).
  - *Note:* there is normally widening of the vertebral canal at both the cervical and lumbar intumescences.
  - The conformation of each vertebra (check for alterations in opacity, shape and margination) (**69**, **70**).
- The width and opacity of disc spaces (**71**).
- The size and opacity of the intervertebral foramina (**71**).
- The opacity and margination of the endplates (**72**).
- Paraspinal soft tissues for: swelling, loss of normal fascial planes and presence of gas/foreign material (**70**).



▲ **67** Lateral radiograph (a) and transverse T2* GRE MR image (b) of the cervical spine of a dog with a comminuted fracture of C2 following external trauma (hit by car). In addition to assessing the stability of the fractures, the degree of spinal cord compression should be assessed. Advanced imaging may be required for this assessment to be performed accurately. In this case, despite the severe fractures, there was minimal overt spinal cord compression and the dog was managed by surgical stabilization of the fracture alone.

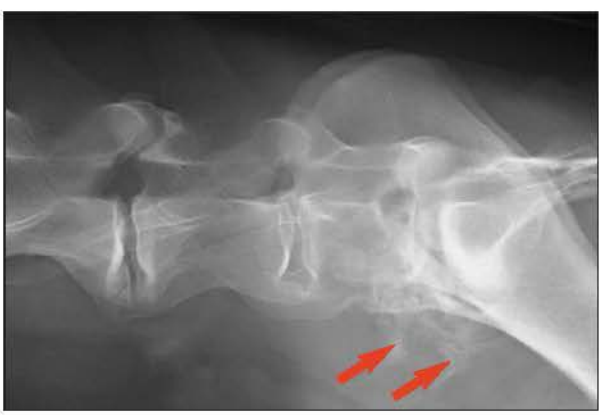


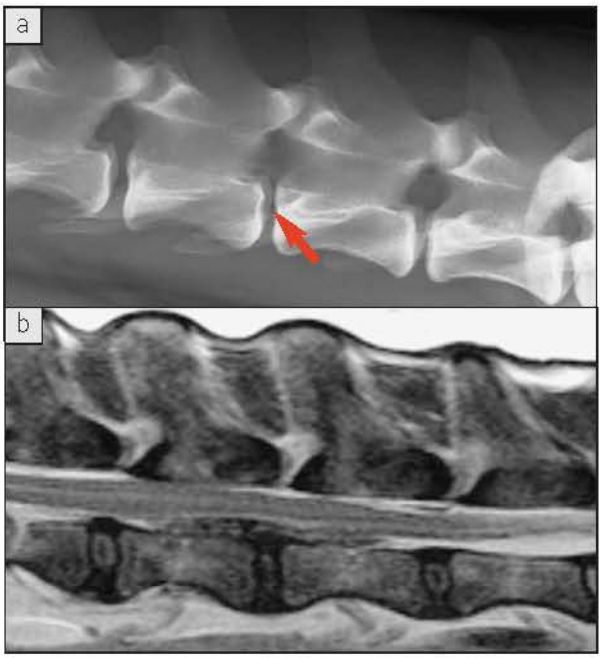
◀ **68** Lateral radiograph (a) and sagittal T2-weighted MR image (b) of a 9-month-old Husky with a 3-month history of progressive ataxia and tetraparesis. The radiograph shows dorsal subluxation of C3 relative to C2. Even without performing myelography or MRI, it is clear that there is significant narrowing of the vertebral canal.



◀ 69 Lateral radiograph (a), transverse CT image (b) and sagittal reformatted CT image (c) of the lumbar spine of a Cavalier King Charles Spaniel with back pain due to lymphoproliferative disease. The radiograph shows multifocal lysis of the vertebral bodies and spinous processes. In comparison, the CT images show much more extensive bone destruction. Radiography often underestimates the extent of bone destruction. Note the loss of the normal thin, sharply marginated dorsal surface of the affected vertebral bodies. This is often a sensitive feature of vertebral body destruction.

▼ 70 Lateral radiograph of an 8-year-old Irish Setter with severe back pain. There is incidental spondylosis deformans visible at L5/6 and L6/7, which has all the characteristics of benign new bone: smooth and sharply marginated with no bone destruction. In contrast, at L7/S1 there is ill-defined wispy mineralization (arrows) that extends into a region of soft-tissue swelling ventral to the lumbosacral junction. This is indicative of a very active bone lesion most consistent with neoplasia. Ultrasound-guided fine needle aspiration confirmed lymphoma. The caudal lumbar spine is a predilection site for bone metastases from prostatic and bladder tumours.





◀ **71** Lateral radiograph (a) and sagittal plane T2-weighted MR image (b) of the lumbar spine of a dog with acute intervertebral disc extrusion at L4/5. The radiograph shows typical features of acute disc disease, with narrowing of the disc space, reduction in size of the foramen and increase in opacity of the foramen. There is also vacuum phenomenon within the disc space (arrow). This is an uncommon but relatively specific feature of acute disc disease. Despite the high suspicion of disc disease based on the radiographic changes, localization prior to surgery needs to be confirmed with either myelography or advanced imaging. The MR image shows the typical appearance of an acute disc extrusion, with amorphous hypointense extradural material lying ventral to the spinal cord and compressing the spinal cord dorsally. Note that on the MR image the vacuum phenomenon is difficult to identify, as mineralization and dense fibrous tissue have similar signal intensity to gas.



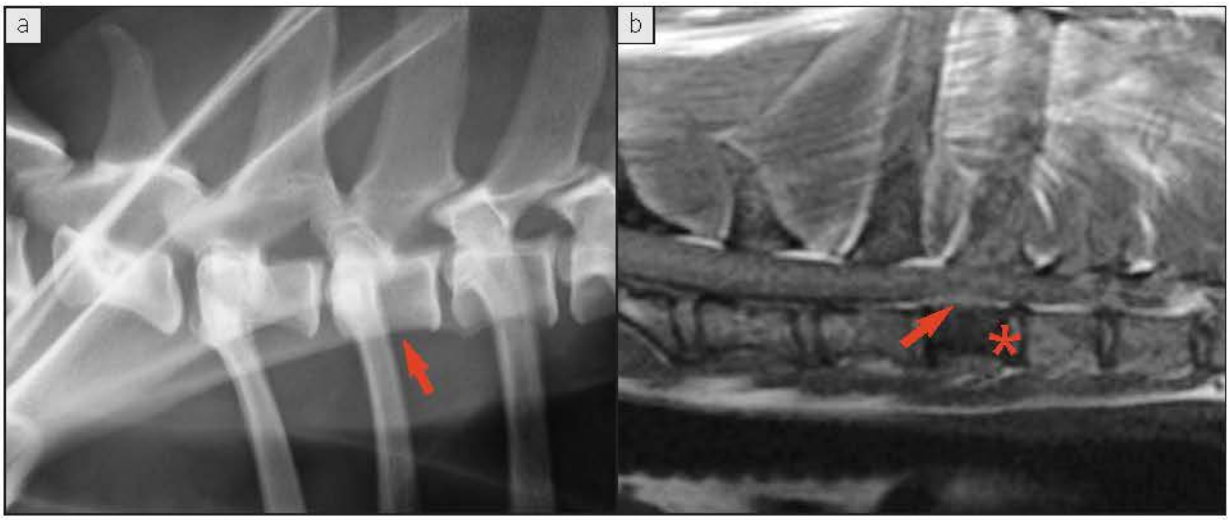
◀ **72** Lateral radiograph of the lumbosacral junction of a dog with discospondylitis of the lumbosacral disc. Note the sclerosis and irregular, 'chewed out' appearance to the endplates and, as a consequence, widening of the disc space. There is soft-tissue swelling ventral to the lumbosacral junction.

Alterations in vertebral alignment

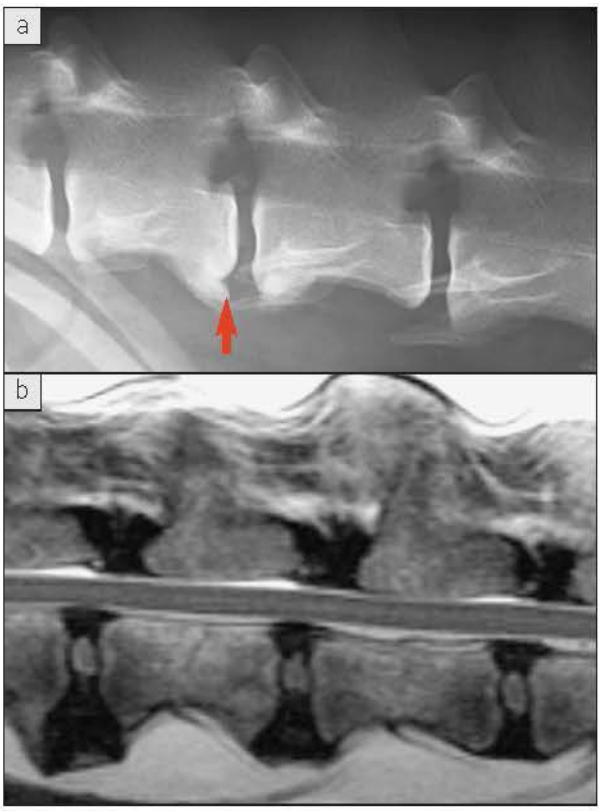
It cannot be assumed that the degree of any subluxation or misalignment on a radiograph correlates with spinal cord injury (unless severe). Often, subluxation/luxation is dynamic and during injury the degree of displacement may have been more marked than is seen on later radiographs. Alteration in alignment may occur due to congenital malformations (e.g. hemivertebrae), fractures, luxations, AA subluxation, scoliosis secondary to syringohydromyelia and caudal cervical spondylomyelopathy.

Alterations in opacity

Radiographs are relatively insensitive for the detection of bone lysis, since at least 50% of mineral must be lost before changes are visible radiographically (**73**). Focal bone lysis is easier to detect than generalized osteopenia and is most commonly a feature of aggressive bone disease (neoplasia or, less commonly, infection). Generalized reduction in bone opacity is most usually seen with metabolic bone disease (e.g. nutritional secondary to hyperparathyroidism) and may result in pathological fractures. Myeloproliferative disease, especially multiple myeloma, may result in 'punched-out' lysis of multiple vertebrae, commonly affecting the spinous processes (**69**). Focal increases in vertebral opacity are usually the result of periosteal new bone and careful evaluation of the periosteal reaction is required to determine the degree of bone activity (**74**) (also **70**).



▲ 73 Lateral radiograph (a) and sagittal T1-weighted MR image (b) of the cranial thoracic spine of an elderly crossbred dog with severe neck pain. The dog has a vertebral tumour at T2. Note the reduced signal on the MR image (asterisk) and the presence of abnormal extradural tissue extending dorsally from the bone (arrow) into the vertebral canal and displacing the spinal cord. On the corresponding radiograph the vertebral body at T2 (arrow) appears largely normal. Radiographs are relatively insensitive for showing bone destruction or infiltrate.



▶ 74 Lateral radiograph (a) of the lumbar spine of a middle-aged dog. Spondylosis deformans is present at the L2/3 disc space. Note the smooth, sharply marginated new bone arising from the ventral aspects of the vertebral endplates (arrow). The new bone production is benign and is usually an incidental finding of no clinical significance. (b) Sagittal T2-weighted MR image of another middle-aged dog with spondylosis deformans. Note that despite the presence of spondylosis the intervertebral discs are normal. The normal intervertebral disc has a hyperintense nucleus pulposus and hypointense annulus.

Disc space narrowing

Narrowing of the disc space usually indicates a reduction in disc volume due to disc disease or, less commonly, a congenitally small disc. The accuracy of disc space narrowing as a sign of disc herniation is only ~70% and false positives are common. False positives may be due to divergence of the x-ray beam, anatomical variants, positioning effects or disc disease not resulting in spinal cord compression. The width of the disc should be assessed by comparison with adjacent disc spaces and care taken with interpretation of disc spaces at the edge of the radiograph. Normal discs have soft-tissue opacity. Chondroid degeneration of the disc nucleus results in early degeneration and mineralization of the disc, which can be considered a normal feature of chondrodystrophic dogs and does not indicate clinically significant disc disease. Dorsal displacement or extension of a calcified disc into the vertebral canal indicates disc herniation, but myelography or advanced imaging is required to assess the clinical significance. In non-chondrodystrophic dogs, discal mineralization is pathological and a feature of disc degeneration, but it may be non-significant. Gas may be present within the disc space. This is known as the 'vacuum phenomenon' and is a specific but insensitive feature of acute disc herniation (**71**).

Interpretation pitfalls are:

- Normally narrowed disc spaces exist at C2/C3.
- Disc spaces in the thoracic spine are most narrow at T10/11 and get gradually wider from T11/12 caudally.
- Wedge-shaped disc spaces can be normal in cats.
- Disc space at L7/S1 is normally wider than other at lumbar discs.

Intervertebral foramina

A reduction in the size of the intervertebral foramina commonly occurs secondary to disc herniation. As the disc reduces in width, the vertebrae move closer together, resulting in reduction in foraminal size. An increase in opacity of the foramina may be seen if a mineralized disc extends dorsally into the vertebral canal where it overlies the foramen. Enlargement of the foramina is rare and can occur secondary to bone remodelling due to pressure from enlarging peripheral nerve tumours/masses or bone lysis due to vertebral tumours. Lysis due to a vertebral tumour is usually irregularly marginated, in contrast to pressure atrophy, in which remodelling is often smoothly marginated, although there can be some overlap.

Interpretation pitfalls are:

- Cervical foramina can only be seen clearly on oblique views.
- Foramina in the mid-lumbar region are naturally larger than those at the thoracolumbar and lumbosacral junctions.

Endplate changes

The normal vertebral endplates are smooth and sharply marginated and the more opaque subchondral bone should be uniform in width. Sclerosis of the endplates often occurs with chronic Hansen type II disc disease. In severe, chronic disc disease with collapse of the disc space there may be remodelling of the endplates, which can become flared and slightly irregular. Differentiation from aggressive disc disease (discospondylitis) can be difficult in these cases. Lysis of the endplates with development of an irregular ragged appearance is typical of discospondylitis (**72**). In young, large breed dogs, osteochondrosis dissecans (OCD) lesions may affect the lumbosacral joint. OCD lesions occur most commonly on the dorsal aspect of the cranial sacral endplate or, rarely, the caudal L7 endplate, resulting in a focal defect in the endplate with a separate osteochondral fragment. Sacral OCD may result in compression of the cauda equina. The usually sharp margination of the lesion, separate OCD fragment adjacent to the endplate defect and involvement of only one endplate helps differentiate OCD from discospondylitis.

Incidental findings

There are a large number of anatomical and degenerative changes that affect the spinal column and which may be mistaken for significant pathology. Congenital anomalies are common and often of no clinical significance. Radiographic changes that are unlikely to be clinically significant include:

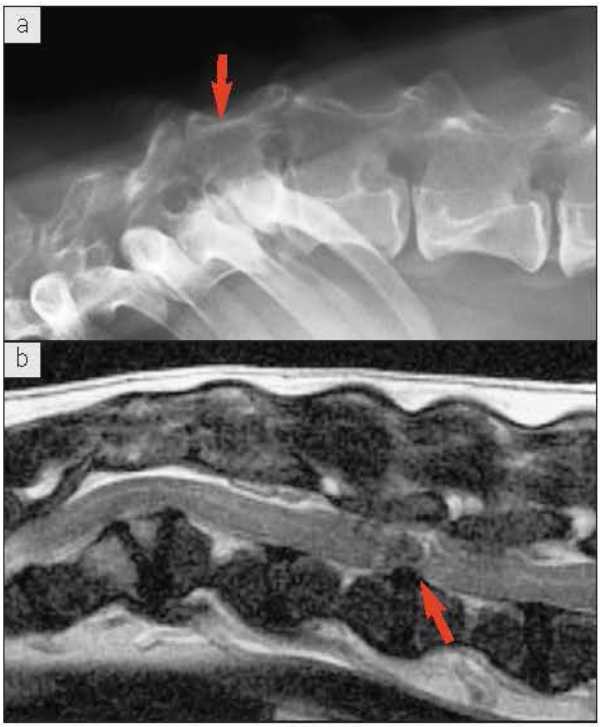
- Transitional vertebrae at the thoracolumbar junction; however, these are important if the last rib is being used as a surgical landmark.
- Spondylosis deformans (unless it extends dorsolaterally to impinge on the intervertebral foramen) (**74**).

- Roughening of the ventral aspect of the vertebral bodies of L3/4 due to normal attachment of diaphragmatic crura. May be mistaken for periosteal reaction.
- Abnormal number of vertebrae.
- Senile osteopenia (cats).
- Block vertebrae, although these may predispose to disc disease at adjacent sites.
- Transitional lumbosacral vertebrae. May predispose to degenerative lumbosacral disc disease.
- Hemi/wedge vertebrae. Common in screw-tailed breeds and often not clinically significant, but can be associated with vertebral stenosis (**75**).
- Dural ossification.

Radiological assessment of spinal trauma

Diagnostic imaging is performed in patients with acute onset of neurological signs or signs following known (or suspected) trauma resulting in neurological signs in order to try and determine the following:

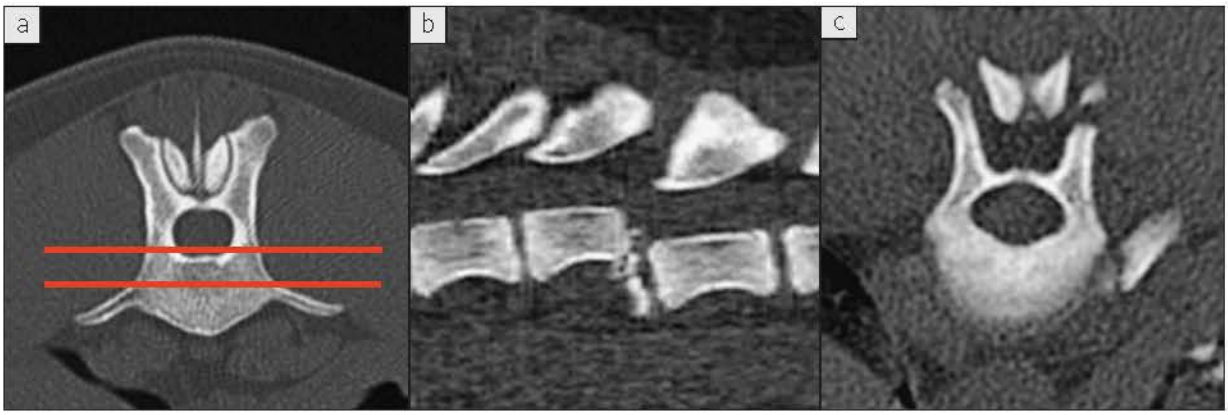
- Whether there are systemic diseases/injuries that require emergency treatment prior to specific investigation of neurological signs (e.g. severe active haemorrhage, pneumothorax, airway obstruction, pleural fluid) (**58**).
- Whether there are severe injuries with a hopeless prognosis (e.g. spinal fracture/dislocation with severe overriding of the vertebrae in a patient with absent nociception) (**76**).
- Whether there are any surgical indications and if so, what would be the best surgical option.
- What the prognosis is.



▲ **75** Lateral radiograph (a) and sagittal T2-weighted MR image (b) of a French Bulldog with acute-onset paraplegia. Note on the radiograph the wedge vertebra at T13 (arrow), resulting in kyphosis. In this case the wedge vertebra did not result in vertebral stenosis (compare with b) and the clinical signs were due to an acute disc extrusion at L2/3 (arrow in b).



◀ **76** Lateral radiograph of the thoracolumbar spine of a dog following external trauma (hit by car). There is a severe, complete fracture-luxation of the spine at the thoracolumbar junction. Due to the degree of overriding it can be assumed that the spinal cord will be transected. Further advanced imaging to assess the spinal cord is not required in this case.



▲ 77 Transverse plane CT image (a) of a lumbar vertebra. The three-compartment model (red lines) can be used to determine if an injury is unstable. Damage to two or more compartments means that the injury should be considered unstable. Sagittal plane reformatted (b) and transverse (c) CT images of a dog with a spinal fracture. All three compartments can be seen to be damaged, indicating that surgical stabilization is required.

Traumatic spinal injuries in small animals can be assessed using a three-compartment model based on a human classification scheme (**77**). The dorsal compartment comprises the articular processes, laminae, pedicles, spinous processes and supporting soft-tissue structures. The middle compartment involves the dorsal longitudinal ligament, dorsal aspect of the annulus and dorsal aspect of the vertebral bodies. The ventral compartment contains the ventral aspects of the vertebral body, lateral and ventral annulus, disc nucleus and ventral longitudinal ligament. If two of the three compartments are disrupted or damaged, the injury is considered unstable (see also **67**). In addition to determining whether the lesion is unstable, the degree of spinal cord compression or narrowing of the vertebral canal needs to be considered. A stable fracture with spinal cord compression due to a bone fragment will require decompression. Survey radiography has relatively poor sensitivity (72%) and negative predictive values (48%) for detecting all vertebral fractures in spinal trauma cases. In particular, there is poor sensitivity for the detection of bone fragments within the vertebral canal (57%) and vertebral canal narrowing (58%), with a negative predictive value of only 35% for identification of spinal cord compression.

Spinal fractures occur most commonly at the junction of mobile and less mobile joints (usually at the cervicothoracic, thoracolumbar and lumbosacral junctions). They may result in compressive and/or non-compressive cord injuries (concussion, contusion, intraparenchymal haemorrhage, laceration). Compressive lesions may be visualized on radiography, but non-compressive spinal cord injury requires advanced imaging (**60, 61**). Survey radiographs should be taken of the entire spine, as multiple fractures may be present. Significant soft-tissue swelling may be associated with cervical spinal trauma, which can result in upper airway obstruction.

MYELOGRAPHY

Myelography may be used for the diagnosis of the site, type and severity of spinal cord compression and, less commonly, cord swelling. Myelography is technically demanding and artefacts are common (**78**), which can make interpretation difficult or impossible. It is relatively invasive compared with MRI and carries a risk of significant side-effects.

The indications for myelography are to:

- Confirm site, lateralization and severity of suspected disc disease seen on survey films.
- Localize the number and site(s) of spinal cord compression or swelling.
- Determine the effect of traction, flexion or extension on spinal cord compression.

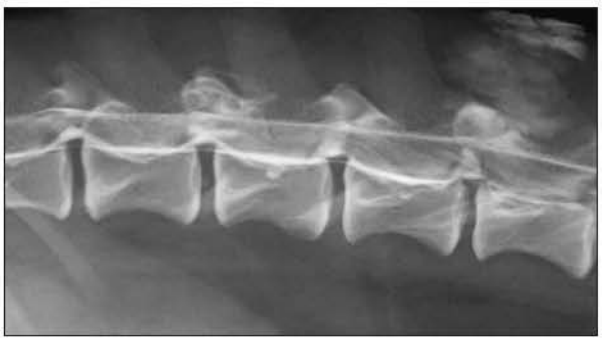
Myelography allows assessment of the entire spinal cord, but as it only allows direct visualization of the subarachnoid space rather than the spinal cord, it provides limited information on the nature of any compressive lesions or cord swelling and minimal or no information on the nerve roots/cauda equina. If the neurolocalization is brachial plexus (focal peripheral C6–T2), cauda equina or a mononeuropathy, advanced imaging is preferred to myelography (**79**). Advanced imaging should be considered if infectious/inflammatory or vascular diseases are suspected.

The risks associated with myelography include:

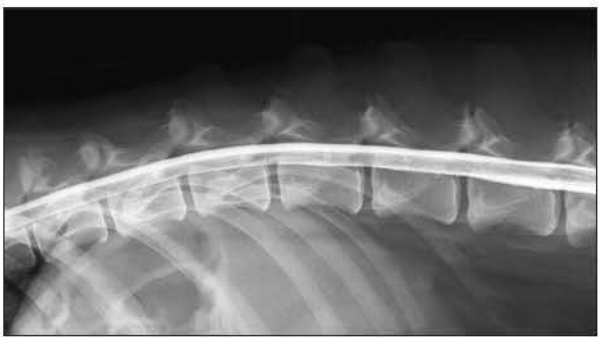
- Seizures post myelography (common; up to 21% in one study and more prevalent in dogs >20 kg bodyweight, with cerebellomedullary injections and with increasing contrast medium concentration).
- Exacerbation/progression of neurological status (usually temporary).
- Iatrogenic injury to the CNS.
- Cardiac arrhythmias.
- Respiratory arrest.
- Death.

The contraindications for myelography are:

- Coagulopathy, including thrombocytopenia and thrombocytopathia.
- Spinal instability (relative contraindication; depends on site of fracture and whether myelography can be performed without destabilizing the spine).
- Cloudy/turbid cerebrospinal fluid (CSF) suggestive of an inflammatory/infectious process.



▲ **78** Lateral myelogram following lumbar injection of contrast. The contrast has gone into the epidural space, resulting in a thick undulating appearance to the contrast and accumulations of contrast at the intervertebral foramina. Epidural contrast leakage or injection is more common with lumbar injections and often results in a non-diagnostic myelogram.



▲ **79** Normal lateral myelogram of a large breed dog. The spinal cord appears as a filling defect between the dorsal and ventral contrast columns. The contrast columns should be assessed for any deviation or changes in width. There are breed and species differences in myelographic appearance, in addition to differences in appearance within a spinal cord region.

Myelographic technique

Prior to injection of the contrast medium, a CSF sample should be taken and examined visually. A cloudy/turbid CSF sample is a contraindication to myelography, which can exacerbate inflammatory CNS disease. If the CSF sample is contaminated by blood during sampling, myelography may still be performed. Iatrogenic blood contamination is usually obvious, as the sample generally starts clear, then a stream of blood is seen swirling within the CSF. If there is doubt as to whether haemorrhagic CSF is the result of iatrogenic blood contamination or due to pathology, then myelography should not be performed until the results of CSF cytology and a white blood cell (WBC) count are available. If the patient may need more immediate treatment based on its clinical signs, a diagnosis should be sought using MRI.

Prior to myelography the contrast medium should be warmed to body temperature to reduce viscosity and minimize side-effects. Survey radiographs should be taken and injection sites should be clipped and aseptically prepared. GA is mandatory for myelography. Spinal needles must be used for myelography, the size of needle depending on the size of the animal, with 22–20g needles most commonly used.

To obtain a diagnostic myelographic study with maximal information, a careful and comprehensive myelographic technique is essential. Following contrast injection, VD, left and right lateral obliques and lateral projections should be taken. Lateral obliques are obtained by positioning the animal for a VD projection then tilting the animal to the left or right by approximately 45°. The contrast medium is denser than CSF, therefore positioning the animal in lateral recumbency, with the affected side being dependent, may improve visualization of the lesion on the lateral projection. The contrast medium rapidly disappears from the subarachnoid space and so the radiographs should be taken as soon as possible after injection.

Only non-ionic low-osmolar iodinated water-soluble contrast medium should be used (e.g. iohexol). The use of ionic contrast media is contraindicated and their injection into the subarachnoid space may be fatal. A concentration of 240–300 mg iodine/ml should be used; higher concentrations are associated with an increased risk of side-effects. The dose of contrast used varies depending on the site of injection, lesion localization and the size of the animal, with larger animals requiring a relatively lower dose. The minimum volume of contrast medium is 2 ml and the maximal dose of contrast medium is 0.45 ml/kg. For regional examinations, a dose of 0.3 ml/kg is normally used and 0.45 ml/kg for examination of the entire spine.

Table 17 **Advantages/disadvantages of the two contrast injection sites used for myelography**

INJECTION SITE	ADVANTAGES	DISADVANTAGES
Atlanto–occipital cisternal injection	• Easier to perform • CSF collection easier and often less blood contamination of the sample • Fewer myelographic artefacts	• Failure of contrast to outline thoracolumbar lesions more common than with lumbar injection • High cervical lesions increase the risk of contrast in the brain • Risk of iatrogenic brainstem injury • Requires an assistant to position the head
Lumbar injection (L5/6 for dogs, L6/7 for cats)	• Can inject with controlled pressure • Position of the needle and contrast can be checked at all times with fluoroscopy • No need for an assistant	• Artefacts (especially epidural leakage) more common • Technically harder to perform, with greater chance of blood contamination • CSF flow can be limited in some patients • Iatrogenic spinal cord injury can occur if needle passes through spinal cord, but this appears to be less of a clinical issue than one would expect; can cause transient LMN dysfunction at the level of the injection • Risk of injection of contrast into the central canal can be clinically significant

Table 18 **Normal myelographic appearance**

Normal myelographic variants

- The ventral contrast column normally elevates dorsally at the cervicothoracic junction
- The ventral contrast column is normally narrower as it passes over C2/3 disc and this should not be mistaken for ventral compression
- In small breed dogs the ventral contrast column may conform to the ventral part of the vertebral canal and narrow as it passes over the disc space
- Breed variation in size of spinal cord relative to vertebral canal (small dogs have relatively larger spinal cords)
- Spinal cord/vertebral canal ratio larger in cervical spine
- Position of dural sac further caudal in small breed dogs and cats compared with large breed dogs
- Dorsal subarachnoid space larger than ventral column in large breed dogs in thoracolumbar spine (**79**)

Spinal cord swelling secondary to large compressive lesions often prevents the passage of contrast following cisternal injections, which may prevent determination of the length of the lesion. Following cisternal injection of contrast the head should be elevated and the x-ray table tilted if possible (lowering the caudal part of the animal) to promote caudal flow of contrast. Following lumbar injection the caudal end of the animal can be elevated to promote cranial flow of contrast. If the cranial and caudal ends of a lesion cannot be assessed, a second contrast injection more cranially or caudally may be required. The choice between cisternal (cerebellomedullary) and lumbar injection sites depends on the suspected site and nature of the lesion. Epidural leakage is a common artefact with lumbar injections. If contrast is injected entirely into the epidural space, then waiting 15 minutes will often result in enough resorption of contrast to allow the injection to be repeated.

The advantages and disadvantages of the two contrast injection sites used for myelography are shown in *Table 17*. The normal myelographic appearance varies with species and patient size (*Table 18*). Care should be taken to avoid misinterpreting normal variants as pathology.

Myelographic interpretation

At least two radiographic projections are required to assess the spinal cord. If the cord is compressed in one plane, the contrast columns may diverge on the orthogonal view. Interpretation of the myelogram is based on classifying the lesions into one of three patterns.

Extradural compression

This results in axial displacement of one or more contrast columns, with narrowing/compression of the spinal cord. On orthogonal views there may be divergence of the contrast columns if compression is severe enough (**80**, next page). Contrast columns are usually thin or partially interrupted at the site of compressions and cord swelling may occur proximal or distal to compression.

The extradural compression pattern is the most common myelographic lesion. Causes include any extradural mass such as disc herniation, vertebral stenosis, vertebral subluxation, neoplasia, haemorrhage, epidural inflammation/infection, foreign bodies and vascular malformations. Myelography determines the location and severity of a compression. Establishment of the differential diagnosis list is based on the additional information provided by survey radiographic findings, history and signalment, clinical examination and other ancillary diagnostic tests. Intervertebral disc herniation is the most common cause of extradural compression. Compared with surgery, myelography has a reported accuracy of 91–100% for the localization of the correct site of disc herniation. Correct lateralization of disc herniation based on the myelographic appearance is less accurate than longitudinal localization, with sensitivity reported to be between 70 and 99%.

Intramedullary swelling

This results in divergence of the contrast columns, which appear thin on all views due to enlargement of the underlying spinal cord (**81**, page 103). Causes include intramedullary mass lesions and any cause of spinal cord swelling (spinal cord neoplasia, acute ischaemic myelopathy, traumatic cord contusion or haemorrhage, syrinx formation and myelitis). MRI is required to characterize the cause of the cord swelling.



◀ **80** Lateral (a), ventrodorsal (b), right ventral–left dorsal oblique (c) and left ventral–right dorsal oblique (d) myelograms of a dog with intervertebral disc herniation at L1/2. Extradural compression with narrowing of the spinal cord is seen on the ventrodorsal and right ventral–left dorsal oblique projections ([b, c], arrows) and divergence of the contrast column on the lateral projection. Note that the right ventral–left dorsal oblique projection shows the maximal cord compression and shows the lesion most clearly. The site of maximal cord compression is dorsal to the disc space and there are radiographic changes consistent with disc disease (narrowed disc space [a], arrow). Given the location, the probable diagnosis is disc herniation, but other extradural masses will result in a similar myelographic appearance.

Intradural/extramedullary lesions

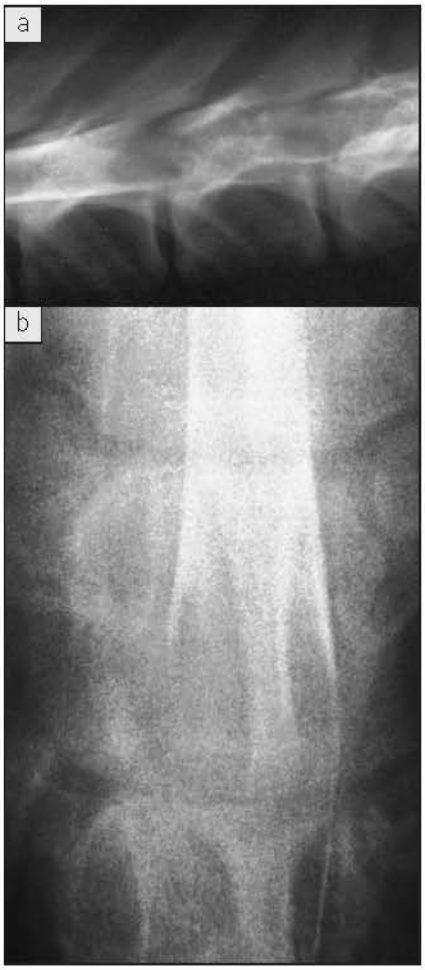
Intradural masses cause filling defects within the dilated contrast columns, resulting in a so-called 'golf tee' sign (**82**), but concurrent epidural and subarachnoid contrast surrounding an extradural lesion may look similar. The splitting or divergence of a contrast column seen with small focal or asymmetrical extradural lesions should not be mistaken for an intradural mass. Localized dilation of the subarachnoid space due to an intraarachnoid 'cyst' or diverticulum formation results in focal widening of the subarachnoid space and narrowing/compression of the spinal cord. These 'cysts' usually have a characteristic teardrop shape (**83**).

Intradural/extramedullary lesions are usually neoplastic, with meningioma and peripheral nerve sheath tumour occurring most frequently, although benign and inflammatory masses can also occur.

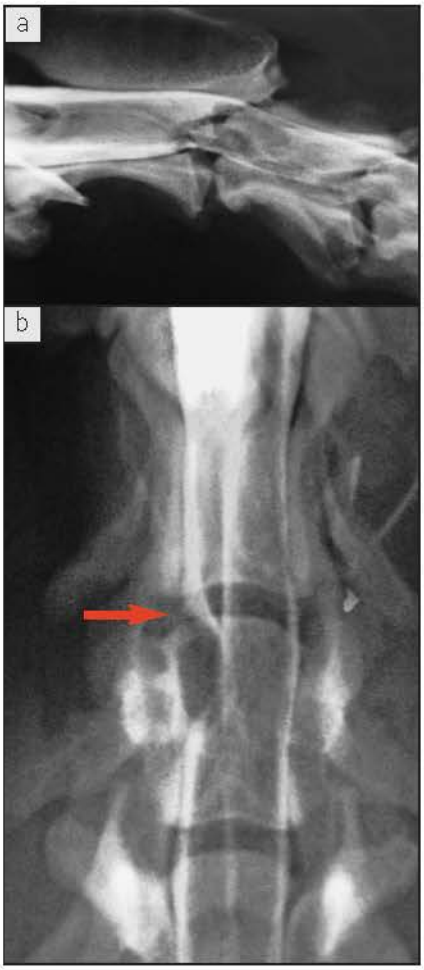
Other myelographic lesions

Extension of contrast medium into the spinal cord may occur with myelomalacia and is a poor prognostic sign. If syringomyelia is present, the syrinx may fill with contrast following direct injection or contrast flowing out along the needle tract.

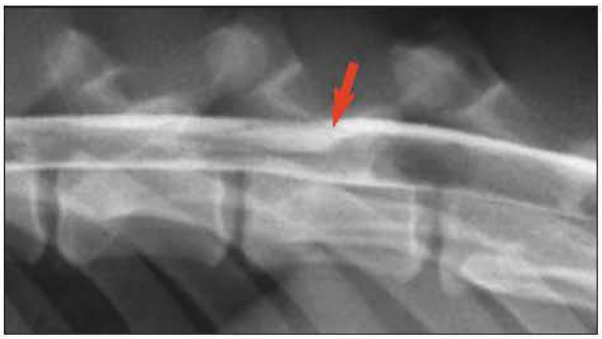
Epidural leakage of contrast medium from the subarachnoid space into surrounding epidural tissue and adjacent soft tissues may occur following dural laceration secondary to spinal trauma or poor technique.



▲ 81 Lateral (a) and ventrodorsal (b) myelograms of a dog with an intramedullary tumour. This is an example of an intramedullary myelographic pattern with divergence of the contrast columns on both projections.



▲ 82 Lateral (a) and ventrodorsal (b) radiographs taken following myelography of a Cavalier King Charles Spaniel with an intradural/extramedullary mass. Note the splitting of the contrast column on the right (arrow [b]) and compression of the spinal cord. The unusual location (dorsal), history and signalment (aged dog) make neoplasia the most likely diagnosis.



◀ 83 Lateral myelogram of a dog with an intra-arachnoid 'cyst'. The finding of a teardrop-shaped dilation (arrow) of the subarachnoid space is pathognomonic for this condition.

ADVANCED IMAGING

Advanced imaging is relatively expensive, but should be performed if:

- Other imaging studies are non-diagnostic.
- Radiography is unlikely to give a diagnosis (brain, soft-tissue lesion or peripheral nerve lesion).
- A more definitive diagnosis is required for prognosis or treatment.

MRI is the imaging modality of choice for neuroimaging, especially for brain and most spinal lesions, but CT can provide useful information and, potentially, a diagnosis in many cases. The physical basis and techniques for performing MRI and CT are beyond the scope of this chapter and the reader is referred to more comprehensive reviews (see Further reading, p. 623).

Imaging technique

Correct neurolocalization and the establishment of a differential diagnosis list are vital before performing advanced imaging to ensure both that the scan is required and that the correct area is being imaged. GA is required for MRI in all but the most stuporous patients. If the animal is a high anaesthetic risk, it should be stabilized prior to scanning. Multislice CT scanners allow fast scanning times, which means that some animals can be imaged under sedation. Ideally, remote anaesthetic monitoring should be used for small animal MRI. If this is not available, the anaesthetist will need to be in the scanning room to monitor the patient.

To accurately assess spinal cord compression, CT is often combined with myelography, with a lower dose of contrast being used. Multislice CT scanners allow high-quality reformatting of the CT images into oblique planes comparable with the multiplanar capabilities of MRI. MRI allows assessment of the spinal cord parenchyma, but with CT this information is limited due to the inferior soft-tissue contrast. As with radiography, careful positioning of the patient is important, as oblique images may be difficult to interpret or completely misleading.

For spinal imaging, animals are best positioned in dorsal recumbency. A plastic radiographic positioning trough may be helpful to prevent the animal from rotating. Alternatively, the body can be supported by foam wedges or bean bags. Very deep chested dogs (e.g. Irish Wolfhounds) may not fit into the scanner in dorsal recumbency, but may be scanned in lateral recumbency using a torso coil. If the patient has to be imaged in lateral recumbency, then careful positioning is vital and the spine will need to be padded as for radiography. It is absolutely vital that the spine is straight. If it is rotated, the patient should be removed from the scanner and repositioned.

As a general rule, T2-weighted MR images are often the most useful for neuroimaging, as they provide the best soft-tissue contrast. On a T2-weighted image, fluid and fat are hyperintense. As most pathology results in an increase in water content, pathology is often hyperintense (bright) on a T2-weighted image.

A routine brain protocol includes transverse pre- and post-contrast T1-weighted, T2-weighted, T2-weighted fluid attenuated inversion recovery (FLAIR), sagittal and dorsal T2-weighted images. In some cases, T1-weighted (post-contrast) images may be useful in the sagittal and dorsal planes (e.g. assessment of the pituitary gland and extra-axial masses). The T2-weighted FLAIR sequence suppresses the signal from CSF and allows assessment of periventricular changes difficult to see on T2-weighted images. This sequence has a high sensitivity for inflammatory CNS disease. FLAIR images are particularly useful if there is hydrocephalus or an intracranial cyst. T2* gradient-echo (GRE) images are very useful for evaluation of haemorrhage or bony changes. In some cases, diffusion-weighted imaging (DWI) may be helpful in the assessment of ageing infarcts and in the identification of small infarcts in the peracute stage. Images acquired with fat suppression (short-tau inversion recovery [STIR] or post-contrast T1-weighted with fat saturation) are useful for showing pathology in the extracranial soft tissues, particularly orbital disease and pathology affecting the bone marrow. In unstable patients, the sequences most likely to give a diagnosis and assess secondary effects of increased ICP should be obtained first (transverse and sagittal T2-weighted images), in case the MRI study needs to be 'aborted'.

For spinal imaging, dorsal plane and sagittal T2-weighted images should always be obtained. If any abnormalities are seen, then transverse T2-weighted images are acquired through the area of interest. If there is any reason to suspect infectious, inflammatory or neoplastic disease, T1-weighted images (pre- and

post-contrast) should be obtained. T2* GRE images are useful for demonstrating bony changes and haemorrhage. In cases of back pain, and as a screening sequence, some form of T2-weighted image with fat suppression/saturation should be obtained. The STIR image is a useful screening sequence, as most pathology results in an increase in signal on T2-weighted images and with fat suppression any lesions within the paraspinal soft tissues or vertebral bodies are more obvious.

Interpretation and assessment of CT and MR images

As with all imaging modalities, the images should be evaluated for technical quality to see if the study is diagnostic and to identify artefacts. The following questions should be answered before interpretation:

- Was the correct area imaged (especially if the image is normal)?
- Were the correct sequences, planes and slice thickness used?
- For CT, have the images been reconstructed to look at the bones and soft tissues in different planes?
- Are any artefacts evident?
- Did contrast enhancement occur as expected?

The questions that advanced imaging and especially MRI can answer include:

- Is there a compressive spinal cord or brain lesion that can be corrected by surgery?
- Is there pathology that can be treated medically (e.g. presence of oedema, inflammatory or infectious disease)?
- How extensive is the lesion?

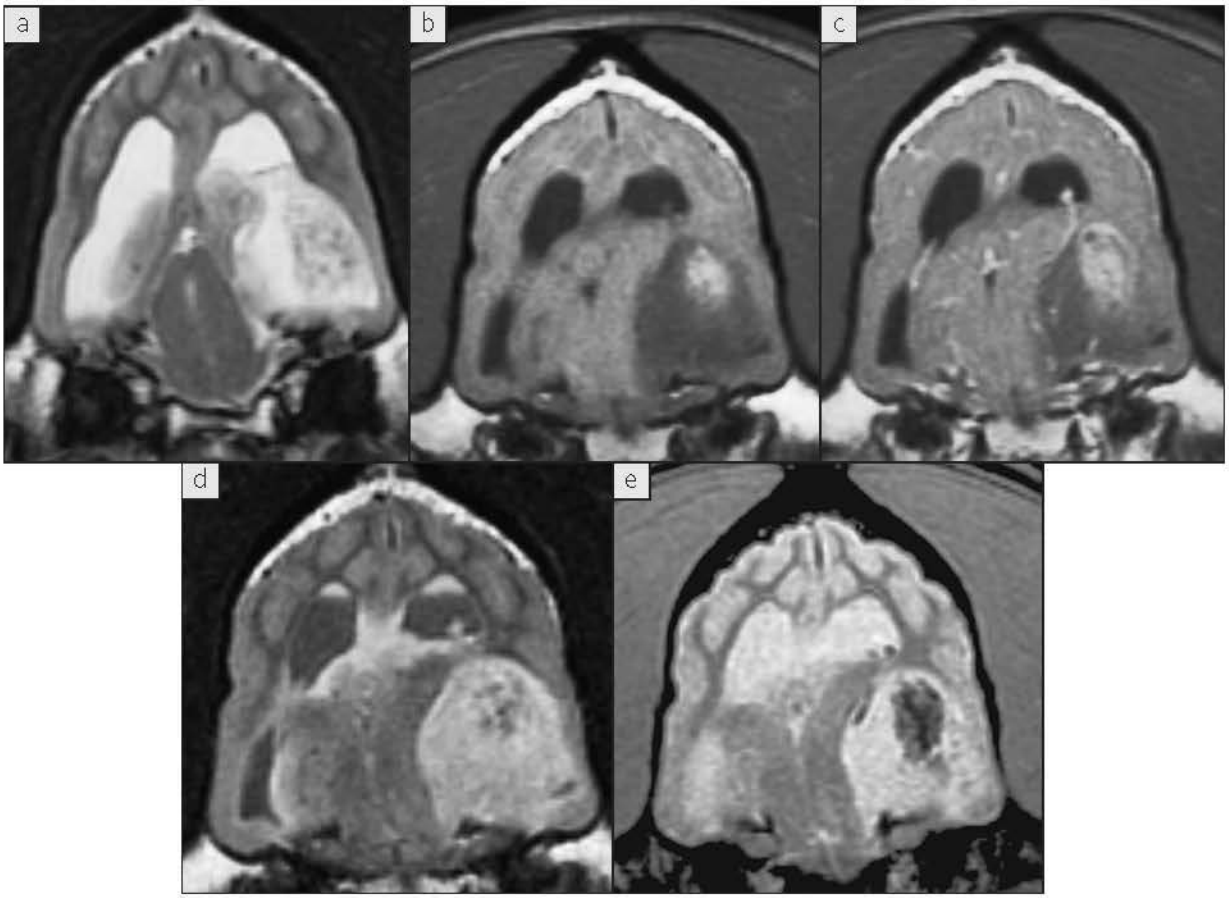
The questions that advanced imaging may provide some help with include:

- Is there evidence of increased ICP?
- What is the nature of the underlying pathology (e.g. oedema, haemorrhage)?

Advanced imaging can also aid in determining a prognosis in conjunction with the neurological examination.

Ideally, CT and MR images should be viewed on a computer work station rather than on hard copy film. The entire film should be read, taking care to look additionally at the peripheral soft tissues. CT images should be reconstructed using bone and soft-tissue algorithms and viewed on both bone and soft-tissue windows. Intravenous contrast (water-soluble iodinated contrast medium [e.g. iohexol]) should be used for most CT brain studies and is often useful for CT studies of neoplastic and inflammatory/infectious diseases of the spine.

Once images have been evaluated for positioning and diagnostic quality, they can be critically assessed. The interpretation of CT and MR images is similar to that for radiography and is based on classical Röentgen signs (size, shape, number, alignment, margination) plus signal intensity or tissue attenuation. Comparison of signal intensity on different pulse sequences allows identification of properties of the tissue (e.g. fatty, cystic) (**84**, next page; *Table 19*, page 107). With CT, tissue contrast is largely due to differences in tissue density. Suspected lesions should be cross-referenced with different imaging planes and sequences, as most genuine lesions are visible on more than one plane. Partial volume averaging is common and can be mistaken for pathology (e.g. apparent defects of skull bones) (**85**, p. 108). The pitfalls in MRI interpretation are detailed in *Table 20*, p. 109.



▲ 84 Transverse T2-weighted (a), T1-weighted (b), T1-weighted post-contrast (c), T2-weighted FLAIR (d) and T2* GRE (e) images of a Boxer with a presumed glial cell tumour within the left piriform-occipital lobe. T2-weighted images have the greatest contrast (fluid is hyperintense) and most pathology is hyperintense on a T2-weighted image. By comparing the lesion on different sequences, information on the tissue characteristics can be obtained. In this case the mass has small cystic regions (hyperintense on the T2-weighted image, which suppress on the FLAIR, and hypointense on the T1-weighted images). There are also regions of probable haemorrhage within the mass (hypointense on the T2* GRE image and mid-hyperintense on T1-weighted images). The FLAIR image shows sediment within the dependent part of the lateral ventricles and an increase in signal within the periventricular tissue that is not visible on the T2-weighted image. This illustrates the value of the FLAIR sequence in cases with pathology affecting the ventricles. In this case the post-contrast images show only minimal/mild enhancement, which is not unusual with intra-axial masses. Contrast medium gives information on the vascularity of lesions and integrity of the blood–brain barrier and post-contrast T1-weighted images should be obtained in all MRI studies of the brain.

Table 19 **Comparison of MRI pulse sequences**

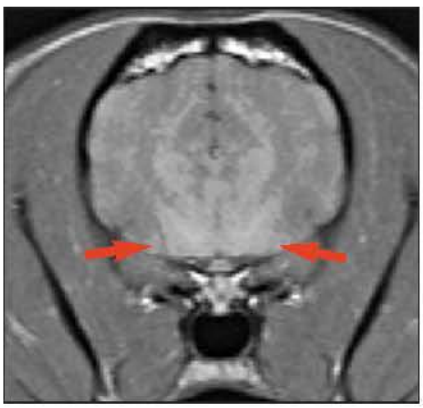
PULSE SEQUENCE	UTILITY	ADVANTAGES	DISADVANTAGES
T2-weighted	High. Should be part of every brain and spine protocol	High. Tissue contrast means very sensitive for detecting pathology	May be difficult to differentiate masses from very extensive oedema. Small lesions adjacent to sulci and ventricles may be missed
T1-weighted	Pre- and post-contrast images are essential for brain studies. Essential in spine if inflammatory/infectious/ neoplastic disease is suspected and for post-surgical evaluations	Good anatomical imaging. Usually used in combination with MR contrast medium (gadolinium chelates). Comparison of pre- and post-contrast images allows assessment of vascularity of lesions and presence of damage to blood–brain barrier	Little soft-tissue contrast
PD	Not useful in comparison with other available sequences	In man may be useful for showing multiple sclerosis plaques. Good anatomical detail, but little advantage over T1W	Time consuming to obtain and offers no significant advantage over T1W
T2-weighted FLAIR	Essential if hydrocephalus, inflammatory/infectious CNS disease or intracranial cystic lesions. Should be part of routine brain protocols. Rarely useful for spinal imaging (occasionally useful to assess cystic spinal cord lesions)	Suppression of CSF signal allows visualization of periventricular lesions, which may be missed on T2W images. Useful for characterization of cystic lesions (will suppress if similar to CSF). More sensitive than T2W images in revealing meningeal disease and may identify small infarcts/inflammatory lesions more clearly than T2W	May be time consuming to obtain. Relatively low signal to noise ratio. CSF flow artefacts may be confused for solid tissue
T2*GRE	Useful if haemorrhage is suspected. Very useful in spine to show bony malformations, bone destruction and production	Most sensitive sequence for detecting intraparenchymal haemorrhage. Small spurs of bone, mineralization and bone destruction often seen better than on other sequences	Susceptibility artefacts at air/bone interfaces and due to microchips/ implants are more marked than with spin echo sequences. This may prevent evaluation of some areas of brain/spine
STIR/FatSat images	Most useful in spinal and orthopaedic imaging. Rarely useful in brain (as limited free fat). Spectral FatSat often used instead of STIR sequence with high-field MR systems	Allows suppression of hyperintense fat signal. This allows visualization of lesions within fatty tissue that may be missed on T2W images (fat and water are both hyperintense, therefore may not detect oedema within bone marrow/fat). Good screening sequence, as quite sensitive for showing lesions in paraspinal soft tissues and vertebrae. Spectral FatSat useful in conjunction with post-contrast T1W images, as allows visualization of enhancement within fat-containing tissues	Time consuming and low spatial resolution with STIR images. Flow within blood vessels may be mistaken for lesions (nerve root masses)

(Continued)

Table 19 Comparison of MRI pulse sequences *(continued)*

PULSE SEQUENCE	UTILITY	ADVANTAGES	DISADVANTAGES
DWI	Occasionally useful to determine age of infarcts within brain. Not useful for spinal imaging	Most sensitive sequence for detecting hyperacute infarcts, which may not be visible on T2W images	Susceptibility artefacts at air/bone interfaces and eddy currents result in marked distortion of image

T2W = T2-weighted; T1W = T1-weighted; PD = proton density; FLAIR = fluid attenuated inversion recovery; T2* GRE = T2* gradient echo; STIR = short-tau inversion recovery; FatSat = fat saturation; DWI = diffusion-weighted imaging.



▲ 85 **Transverse T1-weighted MR image of the brain of a normal dog. Note the blurring and apparent loss of normal cortical bone adjacent to the ventral aspect of the temporal lobes (arrows). The apparent bone loss is artefactual, due to partial volume averaging, and should not be mistaken for skull fractures.**

Assessment of the brain

Assessment of brain images on CT and MRI is mainly based on changes in symmetry (mass effect, loss of parenchyma), changes in the ventricular system, shape and size of the cerebellum and the cranial spinal cord. CT may be of limited value for evaluation of caudal fossa lesions, especially in larger dogs, due to a beam hardening artefact resulting in hypoattenuating streaks, which can obscure pathology. It is important to recognize MRI alterations in signal intensity (grey matter, white matter). CT images should be evaluated for alterations in attenuation of tissues.

The extracranial soft tissues should be evaluated for:

- Muscle volume.
- Muscle signal.
- Nasal or orbital lesions.
- Lymph nodes.
- Changes in skull bones – loss of signal, erosion.

Following administration of MR contrast medium (gadolinium chelates), the images should be assessed to ensure that normal contrast enhancement has occurred. With CT, the normal contrast enhancement pattern is similar to that seen on MRI, with contrast evident in larger blood vessels and in tissues outside the blood–brain barrier. The choroid plexuses, large veins, pituitary gland, nasal mucosa, salivary glands and trigeminal nerve ganglia/periganglionic vascular plexuses should all enhance in a normal animal. Failure of a lesion to enhance post-contrast may be due to lack of a blood supply or an intact blood brain–barrier, but it may also be due to failure of administration of contrast medium

Table 20 Possible pitfalls in MRI interpretation

Ageing changes

Older animals undergo reduction in brain volume and this results in mild widening of the sulci and dilation of the ventricles. Neonatal animals have reduced grey/white matter contrast compared with adult animals due to incomplete myelination at birth

Anatomical variants

Asymmetry of the cranial vault is not uncommon and may lead to distortion of the brain. This can hinder evaluation, but is not significant. It may also make positioning of slices difficult. Mineralization of the falcine meninges may be mistaken for haemorrhage or a small mass lesion

Breed/species variation

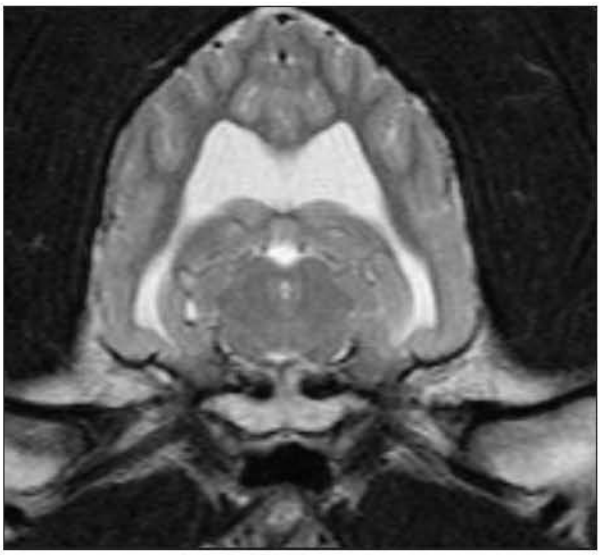
There is marked variation in shape and thickness of the calvarium in dogs. Boxers, Mastiffs and other heavily muscled dogs may have dramatically thicker bone compared with smaller dogs. This should not be mistaken for calvarial hyperostosis. In cats the olfactory/frontal lobes often appear 'pinched' by the medial orbital walls. On sagittal plane images in cats there is often a pointed appearance to the cerebellar vermis. This should not be mistaken for pathological vermal herniation

Ventriculomegaly

Dilation and asymmetry of the lateral ventricles is commonly seen, especially in brachycephalic and toy breeds. Brachycephalic dogs often lack a complete septum pellucidum, resulting in extensive communication between the lateral ventricles (**86**). These dogs are also predisposed to hydrocephalus and the cut-off point where normal ventricular size ends and hydrocephalus begins is unclear. Specific ratios are described, but are rarely used. A rounded appearance to the ventricle and a periventricular halo (seen on FLAIR images) indicates that the ventricular enlargement is pathological (**87**, next page). Dilation of the 3rd and 4th ventricles is abnormal and close examination for an obstructive lesion should be made. Dilation of the olfactory recesses of the lateral ventricles is often seen with significant hydrocephalus

Fluid within bullae

Fluid or tissue in the bullae is not uncommon in brachycephalic dogs (especially Cavalier King Charles Spaniels). This is probably due to primary secretory otitis and is often seen as an apparent incidental finding. Lack of significant enhancement of the bulla wall and involvement of adjacent structures helps differentiate from otitis media

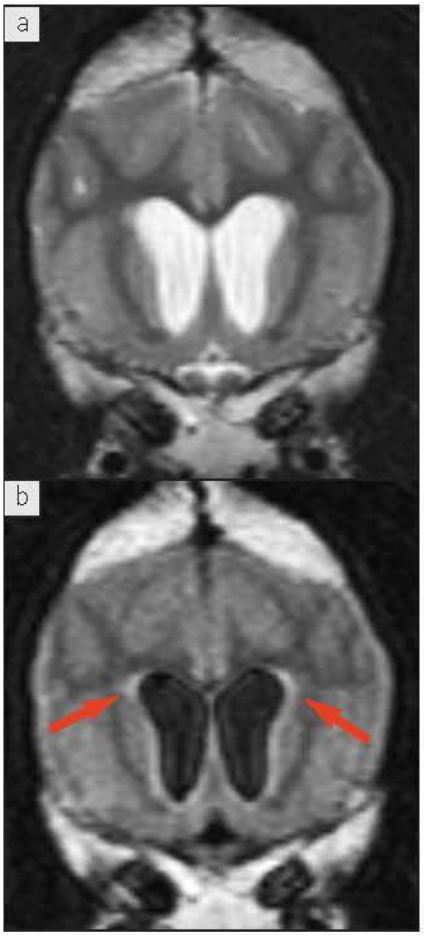


▲ **86 Transverse T2-weighted MR image of a normal Boxer. Ventricular enlargement and asymmetry and absence of the septum pellucidum are common normal anatomical variants and should not be mistaken for pathological hydrocephalus.**

(e.g. contrast still in catheter, leakage from catheter). The mechanism of contrast enhancement is different on CT and MRI. CT contrast enhancement is the result of direct visualization of the contrast agent, whereas with MRI the contrast agent is not directly visualized; enhancement occurs due to the effect of the contrast agent on the immediately adjacent tissues.

Brain masses

Most brain masses are readily identified on MRI or CT images (see also Chapter 26). They are often hyperintense on T2-weighted MR images and are associated with a mass effect (midline shift, compression of ventricles and adjacent parenchyma). Much of the mass effect is often due to perilesional oedema. The presence of oedema is easier to appreciate on MRI than on CT. On CT, oedema results in reduced attenuation of the brain tissue. On MRI, oedema is hyperintense on T2-weighted images, poorly marginated, usually most severe within the white matter and tends to follow the white matter tracts (especially the corona radiata).



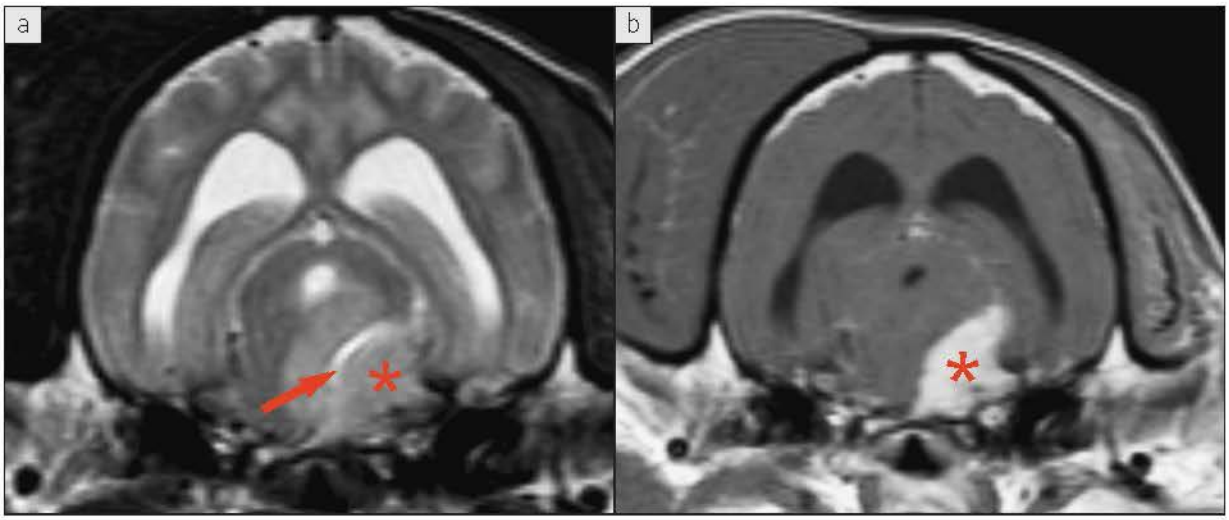
▲ **87** Transverse T2-weighted (a) and FLAIR (b) MR images of a Flat-coated Retriever with obstructive hydrocephalus secondary to an intraventricular mass (not visible). Note on the FLAIR image the hyperintense periventricular halo and rounded appearance to the lateral ventricles (arrows). These features are often seen with an acute increase in intraventricular pressures. The periventricular halo is clearly visible on the FLAIR image, but is difficult to visualize on the T2-weighted image due to the similar signal intensity of the CSF and the periventricular changes.

The differential diagnosis of brain masses is based on classification into extra-axial or intra-axial location. Extra-axial masses arise from outside the neuraxis (e.g. meninges, skull bone) (**88**). Intra-axial masses arise from within the neuraxis (e.g. glial cell tumours) (**84**). Intraventricular masses are classified as extra-axial. The imaging features of masses are non-specific. A mass lesion is not necessarily neoplastic and other causes (e.g. granuloma, haematoma) should be considered. Definitive diagnosis requires tissue biopsy (stereotaxis, free-hand or open surgical biopsy).

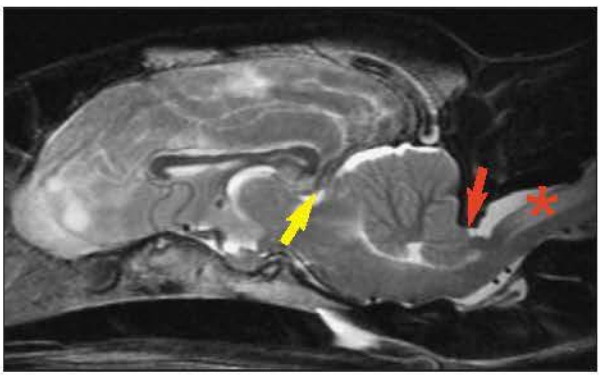
The diagnosis of a brain tumour relies on diagnostic imaging. The aims of imaging an animal with a suspect brain tumour are to confirm the diagnosis, to screen for metastases either to or from the brain and to aid therapeutic planning. MRI also allows identification of the secondary pathological effects of intracranial masses and inflammation (e.g. hydrocephalus, vasogenic oedema, bleeding or brain herniation) (**89**).

Most primary brain tumours in dogs result in no changes to the skull and are not visible on plain radiography. Meningiomas in cats can be associated with hyperostosis of the calvarium, which can be visualized on radiographs, as can areas of mineralization of the tumour. As with any suspected tumour, it is advisable to obtain thoracic radiographs to screen for pulmonary metastases. While primary brain tumours rarely spread to the lungs, metastasis does occur, with consequences for treatment and prognosis. It is more common for tumours to metastasize to the brain than vice versa. Metastases to the brain are less common than primary brain tumours. When they do occur, they are usually multiple, small, located at the junction between grey and white matter (i.e. watershed zone) and surrounded by marked oedema.

Most intra-axial tumours (and other types of brain pathology) result in an increase in water content, which appears hyperintense on T2-weighted images and hypointense on T1-weighted images. Extra-axial masses are variable in appearance depending on cellularity and mineralization. Most extra-axial masses are associated with marked contrast enhancement. The contrast uptake by intra-axial masses is variable (from none to marked). While the mass effect produced by brain tumours is obvious, delineating the mass is not always easy. In some cases of diffuse neoplasia (e.g. lymphoma or gliomatosis cerebri) the changes may mimic inflammatory disease. Definitive diagnosis may require brain biopsy.



▲ 88 (a) Transverse T2-weighted MR image of a dog with an extra-axial mass (asterisk) at the left mesencephalon. Extra-axial masses are typically broad based and lie superficial to the brain and result in displacement of the brain away from the inner surface of the cranium. Note the cleft of CSF between the mass and the brainstem (arrow). (b) The post-contrast T1-weighted image shows dense homogeneous contrast enhancement of the mass (asterisk). The diffuse area of increased signal adjacent to the mass seen on 88a is likely to represent peritumoural oedema.



▲ 89 Sagittal T2-weighted MR image of the brain of a Greyhound with severe meningoencephalitis. As a consequence of the increased intracranial pressure there is subtentorial herniation (yellow arrow) and herniation of the cerebellum through the foramen magnum. Note the rostrocaudal compression of the cerebellum and protrusion of the cerebellar vermis through the foramen magnum (red arrow). Assessment of brain herniation is usually most easily appreciated on sagittal T2-weighted images. Due to the caudal fossa overcrowding, the brainstem is displaced ventrally and compressed and there is swelling and increased signal within the cranial cervical cord (asterisk) due to early syringomyelia/oedema or inflammation.

In addition to identifying the primary lesion, the brain should also be evaluated for secondary pathological effects. Hydrocephalus is commonly seen with masses within the caudal fossa (e.g. brainstem masses) due to compression of the CSF pathways or due to the increased CSF production and protein concentrations seen with choroid plexus masses. With certain tumours (e.g. choroid plexus tumours) treatment may need to be directed to treating the secondary pathological effects. Any disease that increases ICP may result in brain herniation. This is easiest to see on T2-weighted sagittal images, where displacement of the occipital lobes under the osseous tentorium or caudal displacement of the cerebellum through the foramen magnum may be seen.

There are many treatments for intracranial neoplasia and CT or MRI is required in most for accurate treatment planning.

Brain haemorrhage

CT is exquisitely sensitive for the detection of acute haemorrhage, which is evident as increased density due to attenuation of x-rays by the globin portion of blood. The attenuation gradually decreases until the haematoma is isodense at about 1 month after the onset. The periphery of the haematoma enhances with contrast at 6 days to 6 weeks due to revascularization. Until recently, CT was the preferred imaging modality in human patients to determine the presence of haemorrhage in early stroke. Recent developments in MRI mean that CT now offers no advantage in the diagnosis of stroke.

The appearance of haemorrhage on MRI is variable and depends on the age of the haemorrhage, pH, oxygenation, size of bleed and magnetic field strength (see also Chapter 17).

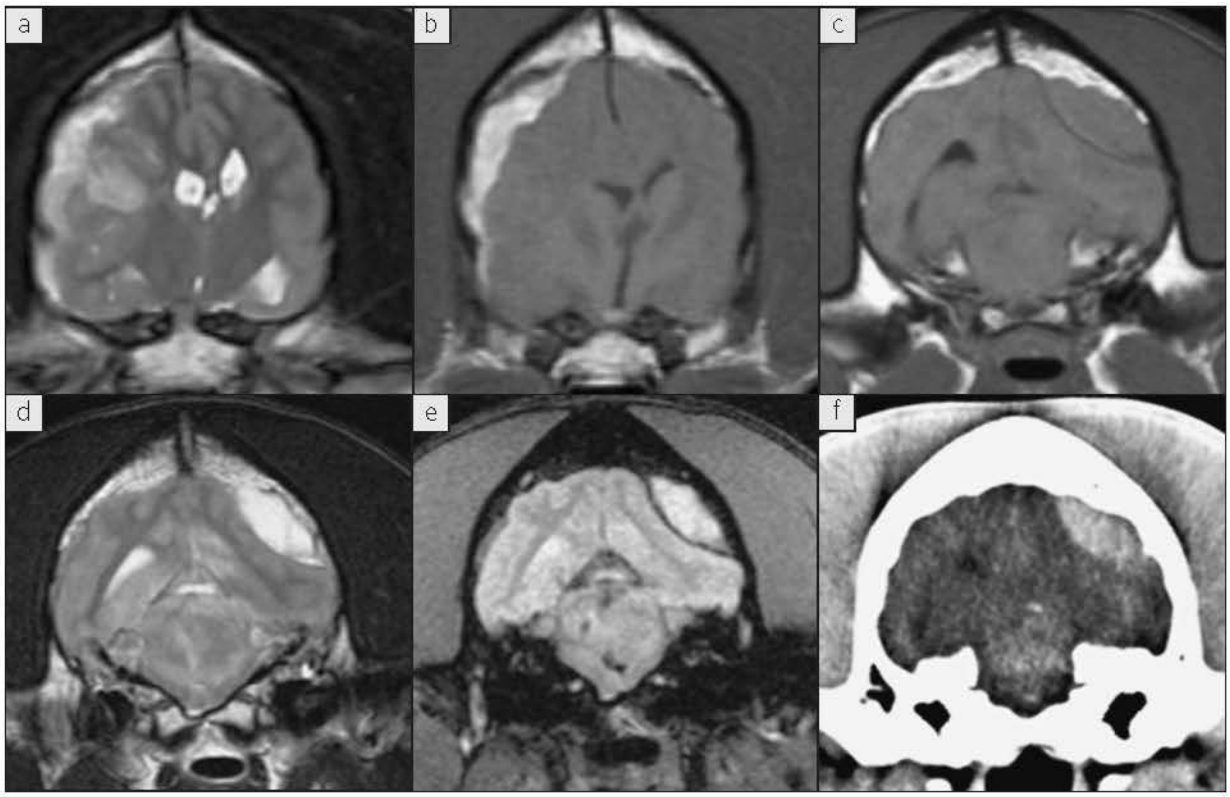
T2* GRE sequences are the most sensitive for visualizing haemorrhage, which always appears as a signal void (black). On spin echo sequences, the appearance depends on the degree of conversion of haemoglobin (*Table 21*).

In small animals the main causes of intraparenchymal haemorrhage are coagulopathy (e.g. primary or secondary to *Angiostrongylus vasorum* infection), neoplasia and trauma. Subdural and subarachnoid haematomas are rare in small animals (**90**) compared to man. Most brain haemorrhage seen in dogs and cats is intraparenchymal. Haemorrhage is commonly seen in association with tumours, but the MRI appearance is predominately of a solid mass rather than a haematoma. Haemorrhagic tumours are often complex masses with solid, contrast enhancing parts (**84**). Lack of a distinct, complex hypointense rim and bleeding of different durations within the lesion are suggestive of neoplasia. In some cases, repeat MRI is required to monitor progression of the lesion. The presence of oedema at a later stage, regression in size of the lesion and failure to follow the expected evolution of a haematoma are indicative of neoplasia.

Large haematomas may show distinct fluid lines. If there is intraventricular bleeding, alterations in signal intensity (decreased signal on T2-weighted and increased on T1-weighted and FLAIR images) and layered fluid–fluid levels within ventricular CSF will be seen. The presence of high signal on a T1-weighted image within the brain and very low signal on a T2-weighted image is suggestive of recent haemorrhage. T2* GRE images are the most sensitive for showing small haemorrhages (which are hypointense). Hyperintensity on a T1-weighted image is not 100% specific for haemorrhage and may be seen with melanin, high protein, flow artefacts and paramagnetic effects (e.g. due to manganese).

Table 21 **MRI signal characteristics of intracranial haemorrhage based on duration of disease**

BIOCHEMICAL FORM OF HAEMORRHAGE	CLINICAL STAGE	DURATION OF HAEMORRHAGE	INTENSITY ON T1-WEIGHTED	INTENSITY ON T2-WEIGHTED
Oxyhaemoglobin in RBCs	Hyperacute	Immediate to few hours	Isointense	Hyperintense
Deoxyhaemoglobin in RBCs	Acute	Hours to days	Iso- to hypointense	Hypointense
Methaemoglobin in RBCs	Early subacute	First few days	Hyperintense	Hypointense
Extracellular methaemoglobin	Subacute to chronic	Days to months	Hyperintense	Hyperintense
Ferritin and haemosiderin	Remote	Days to indefinitely	Iso- to hypointense	Hypointense



▲ 90 Transverse T2-weighted (a) and T1–weighted (b) MR images of a dog with a subdural haematoma secondary to thrombocytopenia. Transverse T1-weighted (c), T2-weighted (d) and T2* GRE (e) MR images and CT image (f) of a Labrador Retriever with a subdural haematoma secondary to *Angiostrongylus vasorum* infection. Hyperintensity on the T1-weighted images and hypointensity on the T2* GRE sequences should raise the suspicion of haemorrhage. Haemorrhage has a fairly predictable evolution on MRI, which can indicate its age. The presence of extensive oedema, contrast enhancement and haemorrhage of different ages failing to follow normal evolution are features of bleeding secondary to neoplasia (84a–e). Acute haemorrhage is hyperattenuating on CT. The MR images show the subdural haematoma clearly (best seen on the T2-weighted image) and the intra-parenchymal bleed (best seen on the T2* GRE). The T2* GRE sequence is the most sensitive sequence for showing haemorrhage on MRI. Most haemorrhage is hypointense on a T2* GRE image, though there are other causes of hypointensity on a T2* GRE image, such as mineralization or gas.

Brain infarct

Brain infarcts in dogs are usually ischaemic with little/no haemorrhage. They are usually arterial and have characteristic imaging findings (see Chapter 17).

CT images are frequently normal during the acute phase of ischaemia, therefore the diagnosis of ischaemic stroke using CT relies on the exclusion of 'mimics' of stroke. Early CT signs of ischaemia can be subtle and difficult to detect, even for experienced readers, and include parenchymal hypodensity, loss of grey/white matter differentiation, subtle effacement of the cortical sulci and local mass effect.

Lesions are most obvious on MR T2-weighted and FLAIR images, where they are usually hyperintense. They have minimal/no mass effect and are usually homogeneous and sharply marginated, with clear demarcation from adjacent parenchyma. Grey matter is most severely affected and lesions are usually confined to one vascular territory.

Territorial infarcts occur with large artery disease and result in large rectangular/wedge-shaped lesions. They are most commonly seen in the cerebellum (small breeds, with Cavalier King Charles Spaniels being predisposed). Large territorial infarcts in the vascular territory of the middle or rostral cerebral arteries are occasionally seen in sight-hounds, among other breeds.

Lacunar infarcts are small infarcts affecting end arteries within deep grey matter structures (e.g. thalamus and caudate nucleus). They are most commonly seen in larger dogs and may be multiple. Chronic lacunar infarcts are sometimes seen as an incidental finding.

DWI is useful in determining the age of the infarct with acute (<9 days old) infarcts appearing hyperintense on the DW image and hypointense on the apparent diffusion coefficient (ADC) map. After 7–9 days the DW image pseudonormalizes. DWI may be helpful in giving some prognostic information if there are multiple infarcts by showing if they are occurring at different time periods. MRI and CT angiography of intracranial arteries is usually of limited or no value for the diagnosis of canine and feline brain infarcts due to the small size of the blood vessels affected, which are often not visible even in normal animals.

Radiography and ultrasonography are useful in looking for the underlying systemic causes of strokes (renal disease and adrenal disease most commonly).

Head trauma

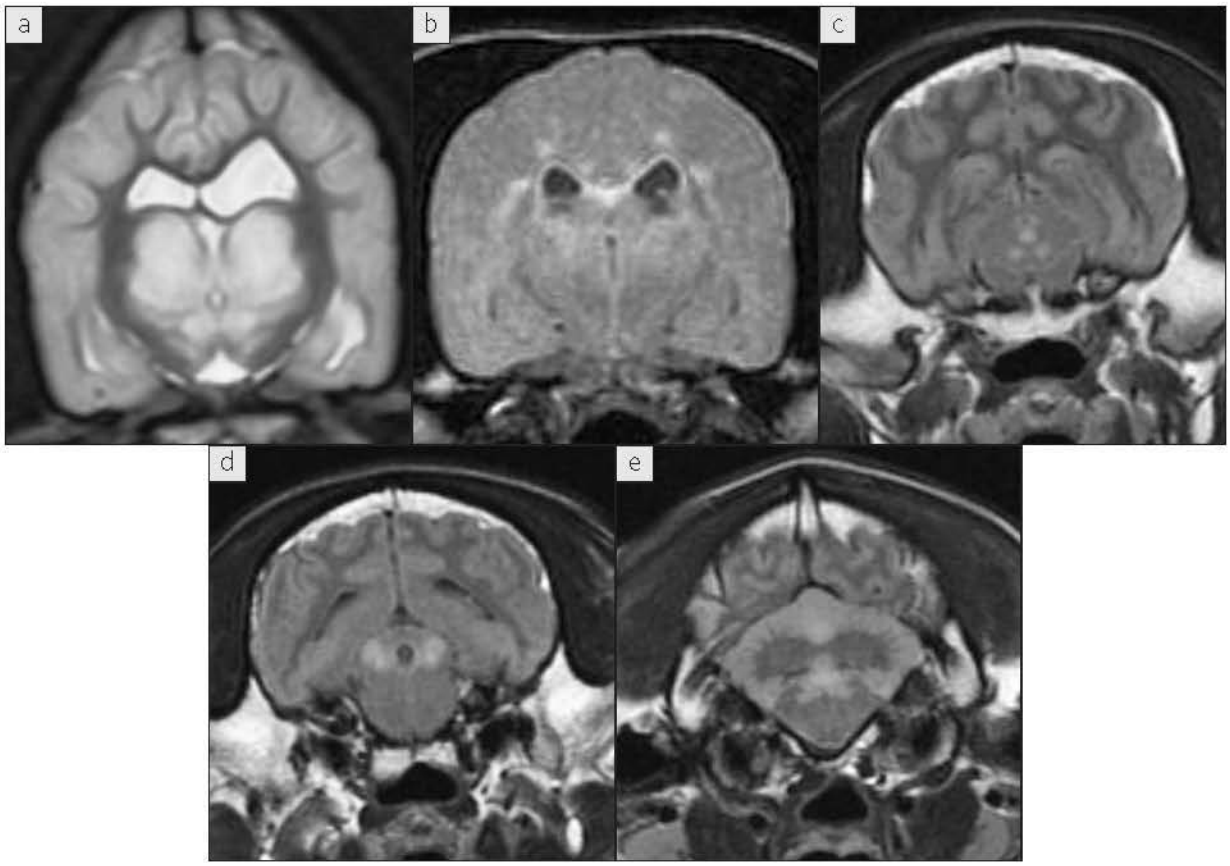
Even mild neurological signs following head trauma have a high incidence of lesions detectable on CT. Most cases of head trauma resulting in neurological signs will have changes on MRI and the imaging study needs to determine if there is significant brain compression due to fracture fragments or haematoma formation or mass effect. A CT examination will clearly show the presence of skull fractures (**62**, p.88) and allow detection of depressed fractures that may need surgical decompression. MRI, while not showing such clear bone detail, gives more information on the extent of brain injury and allows identification of shearing or contusive injuries.

Metabolic/toxic diseases

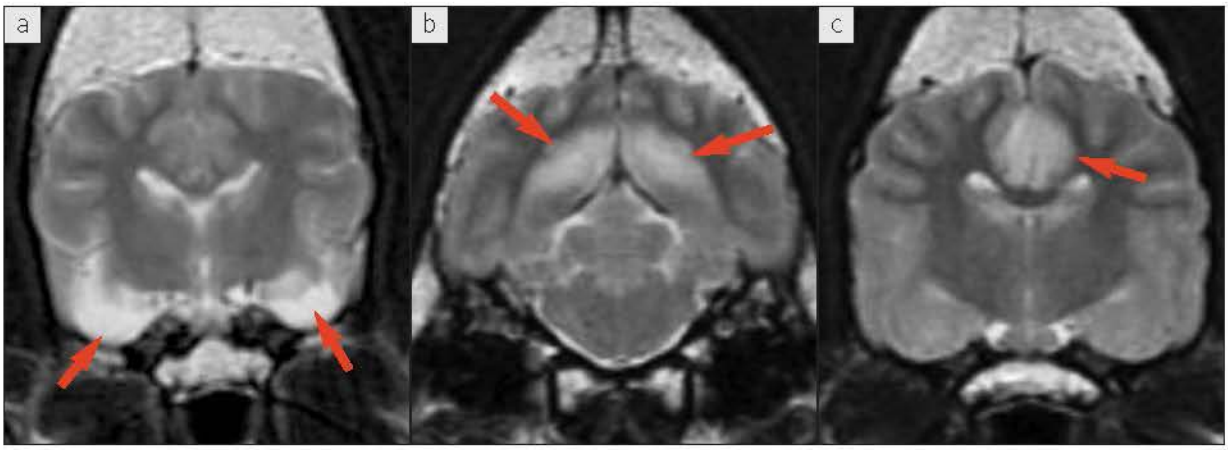
Many metabolic/toxic diseases result in no abnormalities on MRI, therefore a normal MRI examination does not rule out the possibility of a metabolic or toxic brain disease. Diagnosis relies on biochemical testing. Bilaterally symmetrical abnormalities within the grey or white matter are suggestive of a metabolic or toxic aetiology (**91**). The MRI changes most commonly seen with metabolic diseases are hyperintensity on T2-weighted images, with minimal/no mass effect and no abnormal contrast enhancement. The distribution of the lesions is diagnostic for some diseases (e.g. thiamine deficiency). Cortical atrophy and hyperintensities within the lentiform nuclei on T1-weighted images (due to abnormal manganese accumulation) may sometimes be present in animals with congenital portosystemic shunts. Many metabolic diseases occurring in young animals are, however, poorly characterized and the MRI changes may be non-specific.

Imaging findings associated with seizure activity

Idiopathic epilepsy is a diagnosis of exclusion, therefore a normal MRI study is to be expected. If seizures are due to underlying gross structural brain disease, lesions on the MRI examination will usually be obvious (see specific diseases for appearance). There are a number of MRI changes that are thought to be caused by seizure activity. In some dogs with severe seizures an increased signal within the grey matter of the piriform lobe and extending into the hippocampal gyrus may be seen (**92**, page 116). Similar changes in the cingulate gyrus are occasionally seen. The changes in the piriform lobes may be symmetrical or asymmetrical and are best seen on transverse plane T2-weighted FLAIR images. (*Note:* The piriform lobes have slightly higher signal intensity when compared with adjacent parenchyma in normal dogs.) The piriform lobe is also a predilection site for gliomas, which can resemble post-seizure changes. Careful examination should be made for any mass effect. The presence of a mass effect/swelling of the piriform lobe is more suggestive of a tumour than a post-seizure effect. In some cats with seizures, T1-weighted images obtained



▲ 91 Transverse MR image of a Staffordshire Bull Terrier with L2-HGA (L2-hydroxyglutaric aciduria) (a), an English Springer Spaniel with fucidosis (b), and a dog with thiamine deficiency (c–e). Despite the differences in location of the lesions, they all share the characteristics of being symmetrical, hyperintense on T2-weighted images, with minimal or no mass effect, and do not show contrast enhancement. When seen on MRI these features are suggestive of toxicoses or an underlying metabolic disorder. Note that post-seizure changes may resemble a metabolic disorder (92, next page) and bilateral symmetrical hyperintensity may be seen in the white matter of the occipital lobes as an apparent ageing change.



▲ 92 **Transverse T2-weighted MR images of the brain of two different Staffordshire Bull Terriers with post-seizure changes. Note the bilateral hyperintensity within the piriform lobes (arrows) in dog 1 (a) and within the hippocampus (arrows [b]) and cingulate gyrus (arrow [c]) of dog 2. Typically, post-seizure changes are most severe within the superficial grey matter and have no mass effect. The changes may be bilateral or unilateral. CSF analysis +/- repeat MRI scanning is required to rule out inflammatory CNS disease.**

several minutes post administration of contrast may show abnormal diffuse enhancement of the hippocampus. This may also represent a post-seizure change, but the cause is unknown. In some dogs with a long-standing history of seizures, there may be mild atrophy of the piriform lobes/hippocampus. There is no known association between severity and duration of seizures and presence of post-seizure MRI changes. These changes can be detected for up to 10 weeks post seizure in some cases.

Hydrocephalus

In severe cases the diagnosis of hydrocephalus is straightforward on MRI, with obvious marked dilation of the lateral ventricles and thinning of the overlying cortex if congenital in origin. The fontanelle is usually open in toy breed dogs with congenital hydrocephalus, which allows ultrasonography of the brain to identify the enlarged lateral anechoic ventricles. However, this is not always the case, especially if the hydrocephalus is not a congenital lesion. Although the diagnosis may be made with ultrasound in some cases, MRI is indicated to confirm the diagnosis and identify any underlying cause for the hydrocephalus. In most cases of congenital hydrocephalus, only the lateral ventricles +/- the 3rd ventricle are affected. Dilation of the mesencephalic aqueduct and 4th ventricle often indicates obstruction to CSF flow at the lateral apertures of the 4th ventricle or the foramen magnum. Mild hydrocephalus is commonly seen in association with occipital malformation (Chiari-like malformation), but intracranial signs are not usually seen. In older animals, hydrocephalus is often secondary to inflammatory or neoplastic disease. In such cases it is essential that FLAIR images are obtained to identify periventricular lesions. In dogs with choroid plexus tumours and cats with feline infectious peritonitis (FIP) there may be intraventricular masses arising from the choroid plexuses. Seeding along the CSF pathways with lesions in multiple parts of the ventricular system may be seen with choroid plexus carcinomas and FIP. Choroid plexus masses normally exhibit marked contrast enhancement. Dilation of the olfactory recesses of the lateral ventricle and a periventricular halo of increased signal (seen on FLAIR images) are suggestive of increased intraventricular pressure (**87**).

Compensatory hydrocephalus (hydrocephalus *ex vacuo*) is seen secondary to loss of brain parenchyma, with widening of the sulci in addition to the ventriculomegaly. This is most commonly due to chronic inflammatory/vascular disorders and degenerative disease. It is often seen in older animals and is not associated with thinning of the calvarium.

Inflammatory diseases

Inflammatory CNS disease may be associated with a normal MRI examination. In one study, 6 of 25 dogs with inflammatory CSF had a normal MRI examination. Investigation of suspected inflammatory/infectious disease therefore requires CSF analysis.

Meningitis

In many cases of meningitis the CT or MRI images will be normal, with the diagnosis requiring CSF analysis. Unless the meningitis/encephalitis is severe, there may not be changes on T2-weighted images, but FLAIR images may show a thin rim of increased signal representing abnormal meninges. On MR T2-weighted images the chemical shift artefact can mimic meningitis due to the presence of linear hyperintensities at the meningeal/skull boundary. Chemical shift artefact occurs at fat/soft-tissue interfaces and is due to errors in spatial localization resulting from differences in resonant frequencies of fat and water. In cases of meningitis there is often involvement of the pia, which extends between the sulci. Increased signal of the pia on FLAIR images is abnormal and helps differentiate genuine meningeal changes from chemical shift artefact (chemical shift artefact does not extend into the sulci). Post-contrast T1-weighted images are the most sensitive MR sequence for diagnosing meningitis. Abnormal enhancement of the meninges is often seen, but is subjective, and the normal appearance of the meninges varies with the MR machine, the contrast medium used, imaging parameters and the timing of image acquisition following contrast administration. It is helpful to have a normal image to compare, as meningeal enhancement may be subtle. Two patterns of meningeal enhancement are described: dural (no extension into the sulci) and pial (enhancement of meninges extending into the sulci). It is abnormal for the pia to enhance significantly. In severe cases of meningitis, subdural/subarachnoid fluid accumulation may occur between the skull and the surface of the brain. This needs to be differentiated from subdural/extradural haemorrhage (by assessing signal intensity of the fluid), which can provoke a chemical meningitis. Differentiating patterns of meningeal enhancement does not aid diagnosis, as this is a non-specific finding. Diffuse meningeal tumours (lymphoma most commonly) may appear identical to inflammatory disease on MR images. Meningitis is not usually visible on CT without the use of intravenous contrast unless it is very severe or if there are extra-axial fluid accumulations. The appearance of meningitis on CT is similar to that on MRI, with abnormal contrast enhancement seen in severe cases.

Encephalitis

The appearance of encephalitis on MRI is variable and there can often be concurrent meningeal involvement. Most commonly there are multifocal patches of ill-defined hyperintensity on T2-weighted and FLAIR images, with a variable mass effect (from none to marked) (see Chapter 19). In some cases it is impossible to differentiate inflammatory disease from diffuse or infiltrative neoplasia. Conditions such as granulomatous meningoencephalitis (GME) have a predilection for the white matter as well as cerebellum and brainstem. Necrotizing meningoencephalitis occurs in several small breed dogs (Pugs, Maltese) and preferentially affects the cerebrum, with areas of cavitation and cyst formation. Mengingoencephalitis secondary to extension of disease from outside the skull (usually middle ear disease) occurs occasionally, but with extensional disease the extra-axial MRI changes are evident (**63**). The sensitivity of CT for diagnosing encephalitis is lower than that of MRI. Multifocal hypoattenuating lesions with variable enhancement may be seen with encephalitis, but mild cases of encephalitis may have a normal CT scan. In severe cases a mass effect and areas of reduced attenuation due to oedema may be visible. Cats with FIP affecting the brain commonly have obstructive hydrocephalus due to marked inflammation of the meninges and periventricular tissues/ependyma. These changes are clearly visible on MR images, with dilation of the ventricular system and abnormal enhancement of the meninges and periventricular tissues/ependyma. Abnormal CSF signal (increased on T1-weighted and FLAIR images) may be also be seen on MR images due to elevated protein levels within the CSF.

Advanced spinal imaging

Interpretation of spinal CT and MR images

Interpretation of all imaging modalities is based on the classical 'Röentgen signs' of shape, size, number, opacity (or signal intensity) and margination. In addition, for the spinal column attention should be paid to the alignment of the vertebral canal as a whole. Due to the complex geometry of the spine, the importance of high-quality images cannot be overemphasized. Myelography is often required to assess the spinal cord accurately with CT. Intravenous iodinated contrast medium is useful for outlining spinal masses and opacifying the spinal blood vessels, which may delineate compressive lesions.

The following areas should be evaluated on spinal images:

- **Paraspinal soft tissues.** As for the head, assess any changes in muscles and other soft tissues.
- **Vertebral bodies, pedicles, laminae.** Assess the number, shape, size, alignment. Is there any alteration in signal intensity and presence of any cortical destruction?
- **Appearance of the intervertebral discs.** Assess intensity and size of the nucleus, disruption/protrusion of the annulus and any changes (erosion, signal changes) in the endplates.
- **Intervertebral foramina/nerve roots.** Any changes in size, position and signal intensity of spinal nerve, as well as presence of periradicular fat, should be assessed on dorsal, sagittal and transverse planes.
- **Foraminal stenosis.** Frequently associated with loss of periradicular fat (often seen on parasagittal images). Spinal nerves frequently appear swollen, mildly increased in their signal intensity and contrast enhancing with chronic compressions (should not be mistaken for nerve root/spinal nerve tumour). Entrapment of spinal nerve by spondylosis occurs occasionally and this can best be seen on dorsal plane images. It is often difficult with MRI to determine whether the stenosis is due to new bone or soft-tissue hypertrophy.
- **Articular processes.** Assess for degenerative joint disease or associated synovial cysts.
- **Spinal cord.** Assess size (any swelling/atrophy), position, any compression and signal intensity.
- **Subarachnoid space.** Evaluate as for myelography and note any narrowing/divergence of the subarachnoid space.
- **Epidural tissues.** Evaluate the epidural fat and epidural blood vessels for pathological changes.

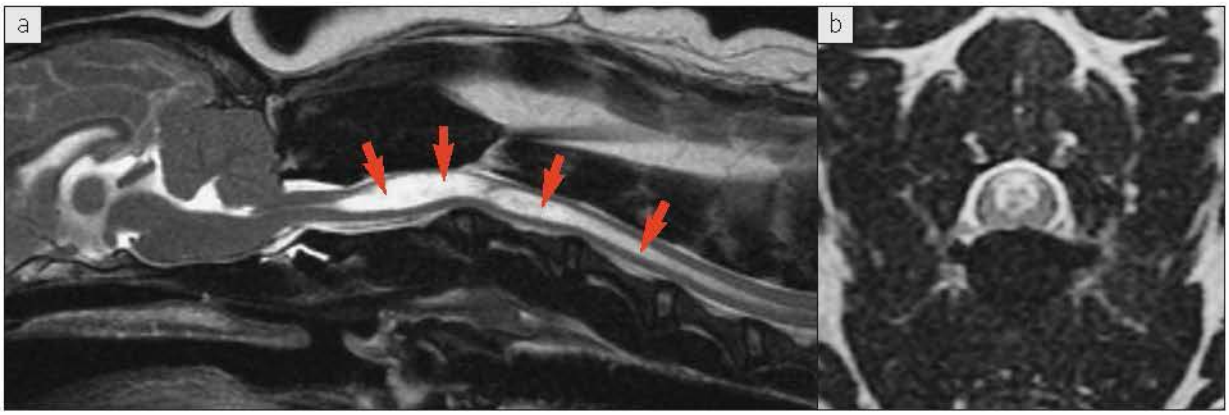
Advanced imaging can provide high-quality images, which means that a large number of incidental degenerative changes may be seen. The significance of imaging findings can only be determined by careful correlation with the neurological and clinical findings. Generally, if there are neurological deficits, then it is more likely that a gross structural lesion will be found. Key questions to answer with spinal CT or MRI include: (a) is there spinal cord compression? (b) what is the severity of compression? and (c) what is the cause of the compression? If the clinical signs are milder or if pain is the only sign, then lesions may be subtle. Spinal pain may be associated with diseases affecting one of many structures, so it is vital to evaluate the entire spinal column and paraspinal soft tissues carefully.

Intervertebral disc disease

MRI is extremely sensitive for detecting degenerative changes of the spinal column, but assessing the significance of any protrusions can be difficult in some cases (*Table 22*). In chondrodystrophic dogs with acute disc extrusion, CT of the spine without the use of intrathecal contrast is as accurate as conventional myelography.

MRI findings

The normal intervertebral disc has a hyperintense (on T2-weighted images) nucleus with a subtle slightly hypointense central cleft seen in some animals. The annulus is hypointense on all sequences; the dorsal longitudinal ligament merges with the dorsal annulus and cannot be differentiated from it. The vertebral endplates are smooth and hypointense on all sequences. With chondroid degeneration seen in chondrodystrophic dogs, there is early dehydration (decreased signal on T2-weighted images) of the nucleus. In non-chondrodystrophic dogs, ageing changes do not occur until middle age. The exception is the lumbosacral disc, which shows signs of degeneration at an earlier age. Calcification of the disc nucleus is difficult to differentiate from dehydration on MRI unless severe (in which case the affected nucleus appears as a signal void). Chronic disc disease is often associated with changes in vertebral endplates and subchondral bone.



▲ **93** Sagittal (a) and transverse (b) T2-weighted MR images of a middle-aged Cavalier King Charles Spaniel with acute-onset neck pain. There is severe syringohydromyelia (abnormal fluid accumulation within the spinal cord parenchyma) (arrows). The spinal cord changes are chronic and in cases where there is acute onset of signs and obviously chronic pathology, alternative reasons to explain the signs should be investigated. Acute decompensation of chronic compressive spinal lesions is commonly seen due to concussion, instability or further compression of neural structures. In this case there was a concurrent foraminal disc extrusion (b). Assessment of the intervertebral foramina in the cervical spine is difficult on sagittal and dorsal plane images. If no lesions are found on these imaging planes, transverse plane images through the disc spaces should be considered.

Table 22 Evaluation of disc disease on MRI

- Position of disc material
- Degree of cord compression
- Nerve root/spinal nerve involvement
- Presence of cord atrophy
- Spinal cord changes – oedema/contusion, gliosis, intraparenchymal
- Complicating factors – subluxation, concurrent syringohydromyelia, vertebral stenosis

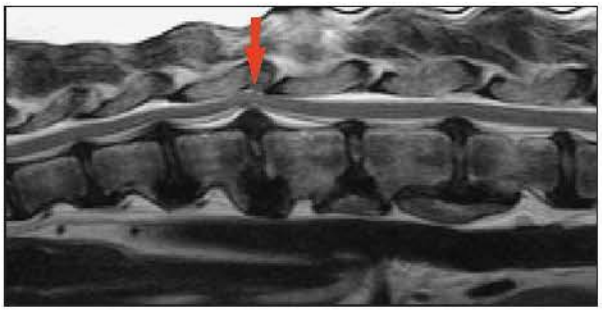
Disc extrusion

Acute extrusions are normally clinically significant and seen as amorphous extradural mass lesions of mid-low signal intensity, extending dorsally from the disc space (**71**). It is difficult to differentiate extruded disc material from haemorrhage; a combination of the two can occur. If vertebral sinuses are damaged, there may be extensive epidural haemorrhage, which can extend for large distances from the site of disc extrusion. This is seen mainly in larger dogs and in the lumbar spine. Epidural haemorrhage appears as amorphous mid-signal tissue, often globular and discontinuous in distribution. Usually the site of the disc disease is obvious and GRE images are helpful to confirm haemorrhage. Haematomas do not usually enhance following contrast administration, but acute disc extrusions may.

Most disc disease is easily seen on sagittal plane images. Foraminal extrusions/protrusions may be missed if only sagittal plane images are acquired, particularly in the cervical spine (**93**). Acute non-compressive nucleus pulposus extrusion may occasionally occur secondary to trauma (**60, 61**), resulting in severe focal parenchymal changes with minimal or no compression.

Disc protrusions

Protrusions are common in older dogs and are characterized by nodules of low-signal disc material protruding through the annulus into the ventral aspect of the vertebral canal and indenting/displacing or compressing the spinal cord. Chronic protrusions are often asymptomatic and are especially common at the lumbosacral junction in older dogs, but they can occur at multiple sites. Spinal cord atrophy is commonly seen on MRI associated with chronic disc protrusions and results in a reduced diameter of the spinal cord (**94**). On myelograms and CT myelograms, preservation of the subarachnoid space may be recognized with spinal cord atrophy. Spinal cord atrophy needs to be differentiated from overt spinal cord compression due to an acute disc protrusion. With spinal cord atrophy there is often well-defined focal increased signal within the spinal cord (primarily affecting grey matter) on T2-weighted MR images and no compression of the dorsal subarachnoid space and epidural fat at the site of reduced spinal cord diameter. With acute spinal cord compression, the epidural fat and subarachnoid spaces are compressed in addition to the spinal cord. MRI signal changes seen with acute spinal cord compressive lesions are usually ill-defined, hyperintense on T2-weighted images and often affect grey and white matter. There may be swelling of the spinal cord cranial/caudal to the site of compression.



▲ **94** **Sagittal T2-weighted MR image of an old Golden Retriever with multiple chronic disc protrusions. The dog presented with acute clinical signs of paraparesis. The image shows chronic disc protrusions with spinal cord atrophy. Note the focal increased signal within the spinal cord and relative preservation of the epidural fat/CSF dorsally despite the severe reduction in spinal cord diameter (arrow).**

Ischaemic myelopathy (fibrocartilaginous embolism)

Radiography of ischaemic myelopathy is usually normal. In severe cases there may be mild swelling of the spinal cord, resulting in an intramedullary pattern visible on myelography. The majority of cases have a focal asymmetrical increased signal within the spinal cord (see Chapter 18). In severe cases there may be mild swelling of the spinal cord. The hyperintensities are irregular in shape and often dorsally located within the spinal cord. The hyperintensity is mainly located within the central grey matter, but may extend into the white matter; however this is difficult to visualize. Within the adjacent spine there are often subtle changes to a nearby disc (often subtle reduction in volume of the nucleus, hyperintense cleft in the dorsal annulus and mild bulging of the annulus). With acute non-compressive nucleus pulposus extrusion the spinal cord changes are similar (although usually they are located over a disc space) and there is often subtle extradural material adjacent to the cord without associated cord compression. GRE images do not show haemorrhage within the cord, which helps differentiate intramedullary disc extrusions. Post-contrast T1-weighted images show variable contrast enhancement within the cord (usually none or mild). Chronic cases of ischaemic myelopathy have more sharply marginated areas of hyperintensity, with no associated swelling representing gliosis or 'cyst' formation on MR images. The majority of animals with suspected ischaemic myelopathy have abnormalities on MRI, although occasionally some dogs may have a normal MRI examination.

CEREBROSPINAL FLUID ANALYSIS

Amy Wood,
Laurent Garosi
& Simon Platt

INTRODUCTION

Cerebrospinal fluid bathes the entire CNS and plays a vital role in its nourishment and protection. CSF originates from a number of sites. Sites of production include: the choroid plexuses of the lateral, third and fourth ventricles; the brain by way of the ependymal lining of the ventricular system and the pial–glial membrane covering its external surface; and the blood vessels in the pia-arachnoid. It is produced both by ultrafiltration from the blood plasma and by active transport mechanisms that utilize energy. CSF is primarily absorbed passively at the arachnoid villi found in venous sinuses and cerebral veins.

CSF normally has a low protein content and contains few cells. Pathology in the CNS is often reflected in the CSF when there is compromise of the blood–brain barrier, the blood–CSF barrier or the CSF's interface with the brain and spinal cord. Abnormalities in the CSF during disease are usually limited to changes in the number and distribution of cells present and increased protein content, making analysis of CSF a sensitive but rarely specific indicator of CNS disease. Because of this, the results of CSF analysis must be interpreted in light of all other clinical findings and, ideally, advanced imaging. Ancillary tests that can be performed on CSF to provide more specific results are covered in the final section.

In the emergency setting, CSF analysis may be indicated in the absence of advanced imaging in cases of suspected inflammatory disease. Additionally, if myelography is to be performed, CSF should be collected prior to contrast injection and preserved for analysis in the event that the myelogram is non-diagnostic.

Table 23 Contraindications for CSF collection

- Patient unstable for general anaesthesia
- Evidence of coagulopathy
- Instability or pathology suspected at the site of collection (e.g. atlanto-axial instability)
- Severe hydrocephalus
- Recent head trauma
- Imaging evidence of intracranial mass lesion or oedema/haemorrhage causing mass effect
- Clinical indication of increased intracranial pressure

General anaesthesia is mandatory for CSF collection. Inherent risks of the procedure include iatrogenic trauma to the brainstem or spinal cord by needle puncture and introduction of infectious agents if there is a break in aseptic technique. Specific contraindications for CSF collection are listed in *Table 23*.

During a spinal tap, the subarachnoid space becomes continuous, via the lumen of the needle, with the outside environment, and the pressure between the two spaces will quickly equilibrate. In the presence of increased ICP, CSF will flow out at a higher rate. This can lead to transtentorial or foramen magnum herniation of neural tissues and acute signs of midbrain and/or brainstem compression. There is not a decreased risk of herniation with a lumbar tap compared with cisternal, as the subarachnoid space is continuous between these two sites of collection.

COLLECTION TECHNIQUE

The site of collection depends essentially on the site of the suspected pathology. As CSF flows predominantly in a cranial to caudal direction, abnormal CSF is more likely to be present caudal to a lesion. An exception to this generalization is in the case of cervical lesions, where a cisternal tap may be of higher yield than a lumbar tap, because the proximity of the cerebellomedullary cistern allows affected CSF to reach it via bidirectional flow.

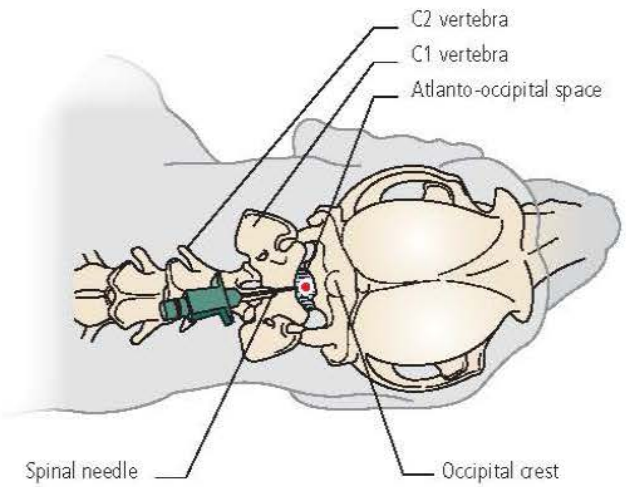
Collection from the cerebellomedullary cistern (CMC, or cisterna magna) is easier and less likely to produce a sample contaminated with blood. This is the most common site of collection in dogs and cats. Lumbar sampling is technically more difficult and more likely to produce blood contamination, but is also more likely to be diagnostically useful for lesions in the thoracolumbar spine.

A minimum of 0.5 ml (approximately 11 drops out of a 22 gauge needle) of CSF is needed for standard analysis by most laboratories. One millilitre of CSF per 5 kilograms of body weight can safely be removed at a time. If CSF is to be sent for analysis to a distant laboratory, two aliquots should be obtained to allow for preservation of one sample (see Sample handling, p. 125).

Cerebellomedullary cistern collection

The animal is anaesthetized and a rigid endotracheal tube is used to avoid occlusion of oxygen flow during the neck flexion required for CSF collection from the CMC. The CMC is reached by inserting a spinal needle at the junction of the horizontal line between the occipital protuberance and the arch of the axis (C2 vertebra) and the vertical line that runs along the cranial edges of the wings of the atlas (C1 vertebra) (**95**). A 22 or 20 gauge 1.5 inch spinal needle will reach the CMC in most dogs and cats, although in large dogs over 30 kg a 2.5 inch needle may be needed.

The region is clipped and aseptically prepared. With the animal in lateral recumbency, an assistant holds the head in ventral flexion (**96**) so that the nose is parallel to the table, while also ensuring that respiration is unencumbered. The animal has to be observed for adequate ventilation during the whole procedure, and positive-pressure ventilation is often required. Adequate depth of anaesthesia should be confirmed before beginning the procedure. The needle is positioned directly on the midline perpendicular to the neck. Once the skin has been penetrated, the stylet can be removed. The needle is then slowly and carefully advanced 1–2 mm at a time. The puncture of the dura mater and atlanto-occipital



▲ **95** The anatomical landmarks for cerebellomedullary cisternal CSF acquisition.

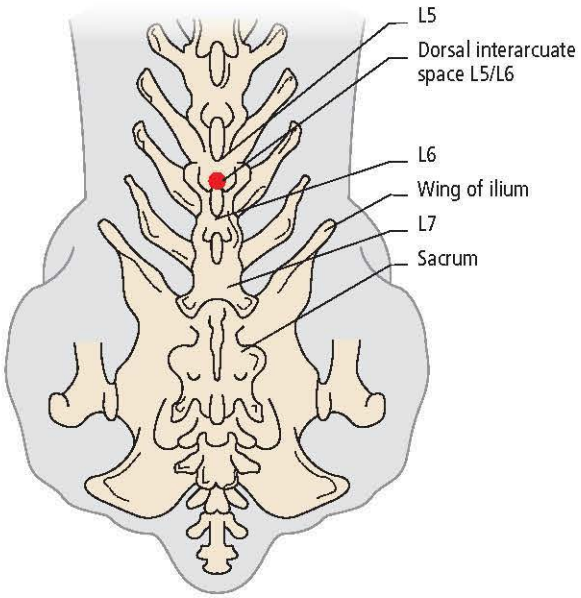


▲ **96** Manual flexion of the head and neck is essential to obtain CSF from the cistern magna. The head is flexed at approximately 90° to the neck in this dog, with the nose parallel to the edge of the table.

membrane may be felt as a slight 'pop', but often this is not the case. Resistance will decrease when the dura is penetrated and CSF flow is observed into the hub of the needle. The flow of CSF is the only reliable sign of a successful puncture. The first two drops of CSF are allowed to drip freely to remove any debris collected during needle insertion, and the following drops are collected into a sterile collection tube. CSF should never be aspirated with a syringe, as this creates negative pressure in the subarachnoid space and increases the risk of herniation.

If the needle hits bone while being advanced, it may be redirected cranially or caudally, moving the needle off the bone into the atlanto-occipital space. If the nose is not exactly parallel to the table, one of the vertebral sinuses will be entered and blood will be obtained instead of CSF. Hitting a vertebral sinus will not prevent getting a clear CSF sample on a subsequent attempt, as these structures are extradural. If blood-tinged CSF is observed initially, it may clear after several drops if it is due to injury to a subarachnoid vessel; it can then be collected. If the blood tinge does not clear, it is probably a result of the disease process and the CSF should be collected for analysis. Once an adequate amount of CSF has been collected, the needle can be slowly withdrawn.

Certain disease processes can obliterate the CMC or increase the viscosity of the CSF to the extent that it will not flow and may not even appear in the hub of the needle. The clinician must be aware of this possibility and not insert the needle too far while waiting for the CSF to appear in the hub. In cases where a CMC sample cannot be obtained, a lumbar puncture can be performed instead.

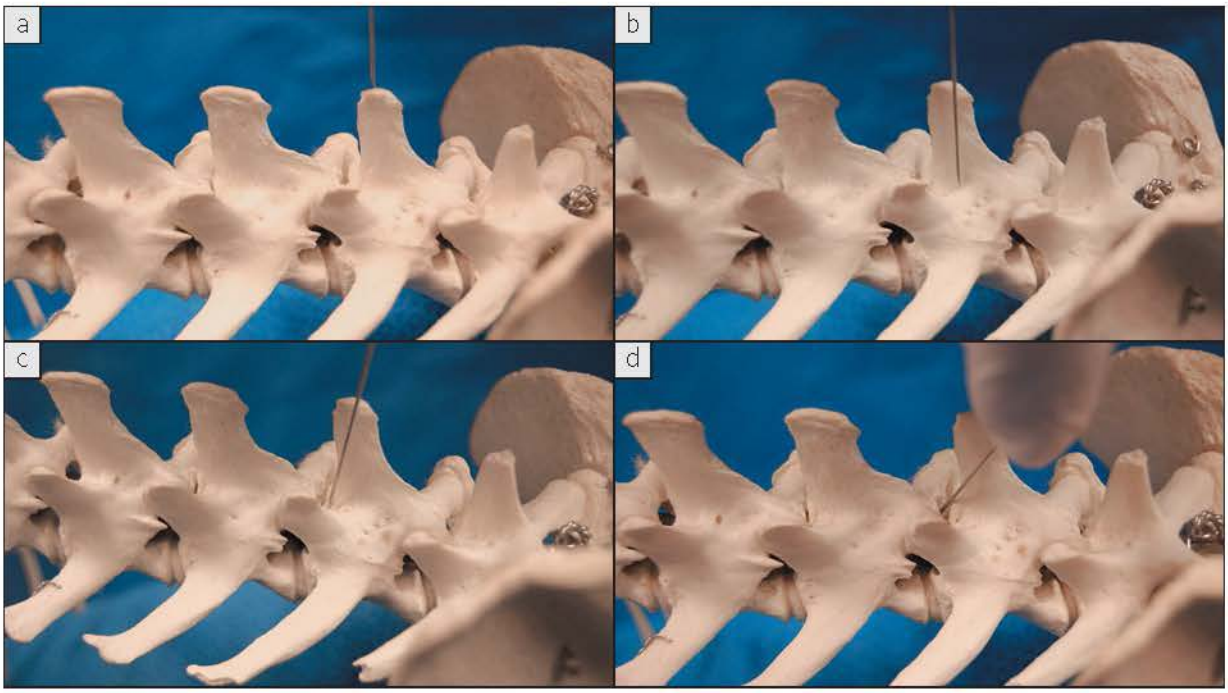


▲ **97 The anatomical landmarks for lumbar CSF acquisition. The L6 spinous process can be found just cranial to the wings of the ilium. For an L5/L6 lumbar puncture, the needle is inserted craniomedially towards the L5/L6 interarcuate space delineated by the caudal edge of the L5 lamina and the cranial edge of the L6 lamina.**

Lumbar collection

Lumbar puncture is technically more difficult than CMC puncture and is more often associated with blood contamination. The site for lumbar puncture is L5/L6 (or L4/L5) in dogs and L6/L7 (or L5/L6) in cats. The area is clipped and aseptically prepared. The patient should be positioned in right lateral recumbency (can be in left lateral recumbency for a left-handed person) so that its dorsum is close and parallel to the edge of the table. The hindlimbs are flexed as much as possible. The L6 spinous process is palpated just cranial to the wings of the ilium. It is much more prominent than the smaller L7 spinous process caudally (**97**).

The needle is inserted, with the stylet left in place, over the centre of the spinous process of L6 if attempting



▲ 98 **Placement of the spinal needle into the lumbar subarachnoid space is depicted in this sequence. (a) The spinal needle is positioned on top of the dorsal spinous process of L6 following manual localization of this process using the wings of the ilium. (b) The spinal needle is 'walked down' the lateral aspect of the spinous process until it reaches the dorsal lamina of the vertebra. (c) The needle is then angled cranially and slightly medially while advancing cranioventrally. (d) The needle will move through the soft tissues of the interarcuate ligament and should be advanced until it hits bone, which should be the floor of the vertebral canal.**

to reach the L5/L6 space and advanced until it hits the spinous process (**98a**). The needle tip is then moved slightly laterally so that it can be 'walked' down the spinous process until it hits the dorsal lamina (**98b**). It is subsequently advanced at a 45° angle with the needle point directed cranially remaining against the spinous process (**98c**). When correctly positioned, the needle typically passes through the interarcuate and yellow ligament; this feels as if the needle is going through rubber. This step is performed 'by feel' and multiple attempts may be necessary to achieve the correct angle of insertion. If the needle hits bone while being advanced, it may be redirected cranially or caudally, moving the needle off the bone into interarcuate space while remaining alongside the spinous process. This may lead to bending of the needle, so a 20-gauge needle is often required in larger dogs (2.5 or 3.5 inch). If it is no longer possible to visualize the tip of the needle in relation to the anatomy, the needle should be withdrawn for a new attempt.

The needle will pass through the yellow ligament and the cauda equina/caudal spinal cord. The latter often results in a tail or leg twitch seen or felt by the holder. The needle is advanced to the floor of the vertebral canal (**98d**). When the stylet is removed, CSF flow is observed, which is the only reliable sign of a successful puncture. CSF may be collected from either the dorsal or ventral lumbar subarachnoid space. If CSF does not appear, the needle can be withdrawn slightly off the floor of the canal or carefully turned while in place.

If blood appears, the needle should be withdrawn and a new attempt made. If blood-tinged CSF appears, it may clear in a few drops. If the blood tinge does not clear, it is probably part of the disease process and the CSF should be collected. Complications of passing the needle through the caudal spinal cord and nerve roots are occasionally reported, but this procedure can cause intradural or intramedullary haemorrhage.

SAMPLE HANDLING

CSF should be collected into an empty sterile container. If infection is suspected, CSF can be collected into culture medium or a culturette swab can be used to take a sample out of a sterile container. (See Standard analysis techniques, for samples that are to be analysed in-house rather than sent to a commercial laboratory.)

If analysis is going to be delayed by more than an hour, ideally at least two aliquots of CSF should be collected: one for analysis of protein, other analytes and cell counts; and one for cytological analysis. Because of the typically low protein content of CSF, the cells in a sample are labile and short-lived once collected, which can significantly alter the differential cell count and reduce the usefulness of the test. Samples with a high protein content (>50 mg/dl) are unlikely to be affected by 8–12 hours of storage without a stabilizing agent, but because the protein content is unknown at the time of collection, a stabilizing agent is recommended. Alternatively, slides can be prepared using one of the techniques described below and mailed to a laboratory for staining and evaluation.

Autologous serum (added to achieve a concentration of 10%), hetastarch (added 1:1) and EDTA (added 1:1) are recommended as stabilizing agents to preserve cell integrity for up to 48 hours after collection. Formalin is not recommended as a preservative if cytological analysis is to be performed; added 1:1 it will suffice for cell count and protein analysis. If too little CSF is collected to submit two separate aliquots, hetastarch should be used to preserve the sample. Protein analysis will not be affected by the addition of hetastarch as it would by the addition of autologous serum or EDTA.

Samples should be clearly labelled when sent to the laboratory so that the dilutional effects of the stabilizing agent can be taken into account when necessary. All samples should ideally be sent at a refrigerated temperature (4°C).

STANDARD ANALYSIS TECHNIQUES

Standard tests performed on CSF include its gross physical appearance (colour and turbidity), quantitative analysis (RBC count, total nucleated cell count [TNCC] and protein concentration) and cytological analysis (leukocyte distribution and characterization in addition to the presence of other cells or infectious agents). Normal values for these tests are given in *Table 24*. Ideally, CSF should be sent to a commercial laboratory with the necessary equipment to perform these tests, established reference intervals and clinical pathologists experienced at interpreting cytological preparations. However, if this is not possible, many if not all of these tests can be approximated using standard equipment in most clinics, with the caveat that cell counts and cytological analysis of CSF require practice. The cytological appearance of various cell types is beyond the scope of this book, so the reader is directed to other sources (see Further reading).

Macroscopic evaluation

The gross examination of CSF involves assessing it for clots and holding the tube against a white background to assess it for colour change; black print should be read easily through the tube as a test of clarity. Turbidity can occur once the TNCC is in excess of 500/µl.

Table 24 **Expected normal parameters for CSF analysis**

PARAMETER	NORMAL FINDING
Colour/clarity	Clear and colourless
Total protein	<25 mg/dl (cisternal) <45 mg/dl (lumbar)
Red blood cells	Not normally found (excluding iatrogenic blood contamination)
Total nucleated cell count	<5 cells/µl
Differential cell count	Small lymphocytes (60–70% in dogs; 15–30% in cats); monocytes (30–40% in dogs; 50–80% in cats); non-degenerated neutrophils and eosinophils (<2%); other non-pathologic cells (rare)

Table 25 Interpretation of urine dipstick readings for CSF protein analysis

DIPSTICK READING	PROTEIN CONCENTRATION (mg/dl)
0 or trace	<30
+	30–100
++	100–300
+++	300–2000
++++	>2000

Protein concentration

The concentration of protein in CSF (sometimes called the microprotein concentration) is very low and is comprised almost entirely of albumin. It is normally higher in the lumbar sample than the CMC one (see *Table 24*). Unlike the cytological analysis, the protein analysis is not time dependent. Because of its low concentration, specialized techniques and reagents (Coomassie blue or pyrogallol red) are needed for quantitative protein analysis. The protein concentration in CSF is too low to be quantified using refractometry, but in-house semi-quantitative approximation of the protein content of CSF can be performed using a standard urine dipstick protein pad. (See *Table 25* for the interpretation of urine dipsticks, bearing in mind that dipsticks are more efficient at detecting albumin and may give a false-negative result in cases of increased globulins.) Protein can reliably be considered elevated based on a dipstick reading of 2+ or greater.

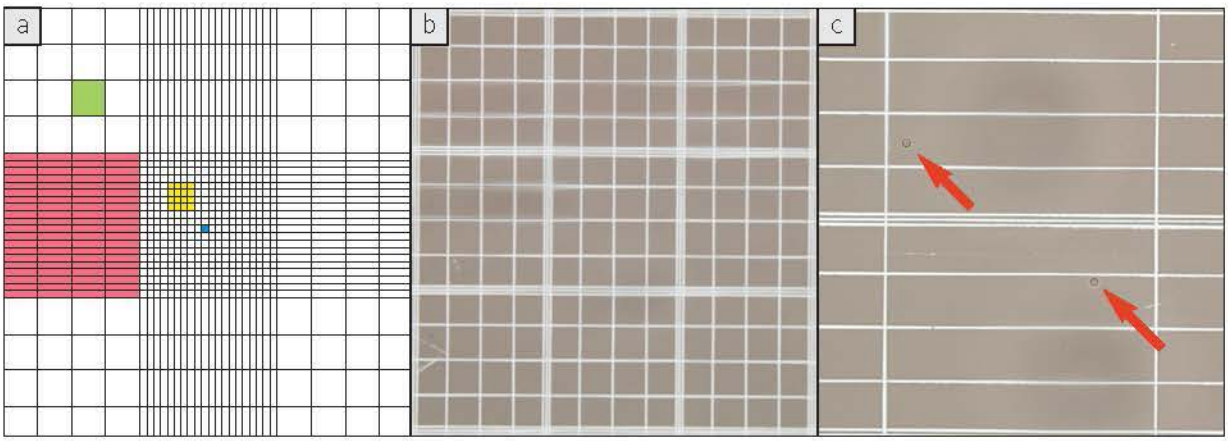
Cell counts

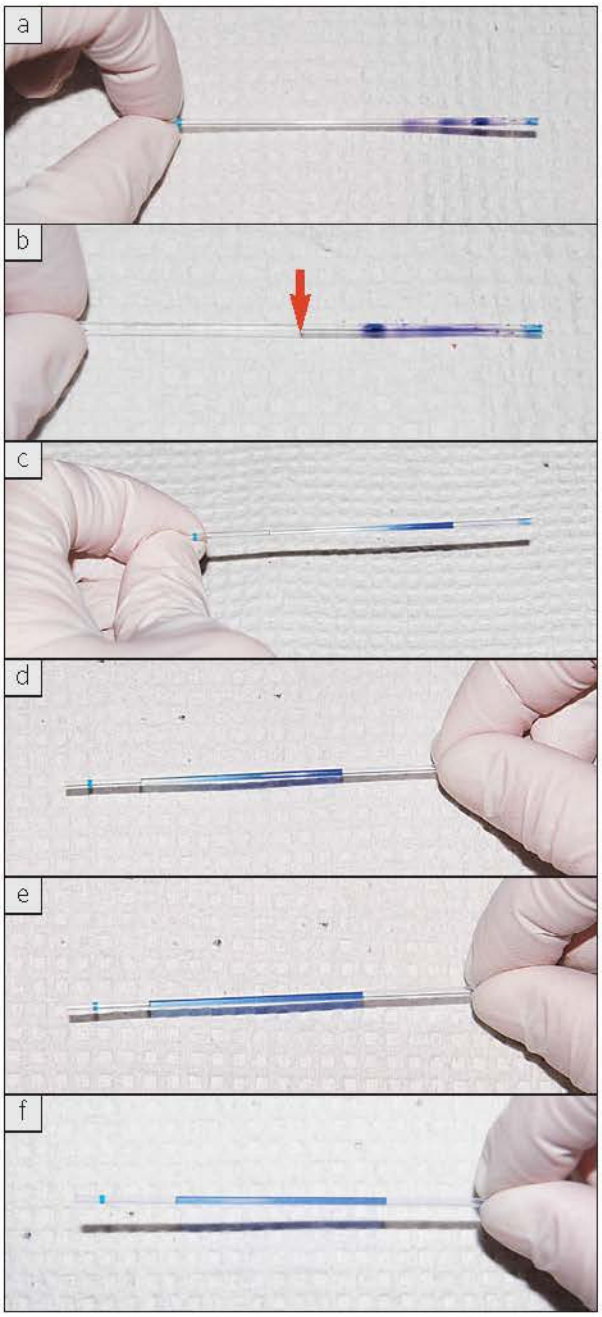
Erythrocyte counts and TNCCs are most commonly performed using the standard haemocytometer technique. This technique is described in *Table 26*. The layout of a haemocytometer chamber is shown in **99**. Though the data have not yet been published, coating the cells with new methylene blue (**100**), as described in steps 1 to 5 of *Table 26*, does not affect the cell counts and makes distinguishing RBCs from WBCs easier. This creates a very practical and feasible approach to a rapid approximation of RBC and WBC counts on an emergency basis.

Leucocytes have a granular, stippled appearance and are usually larger than erythrocytes. Erythrocytes are translucent and biconcave; they lack any internal structures and may have crenated, spiculated edges. Small lymphocytes can easily be mistaken for erythrocytes by the untrained eye.

Though it remains the gold standard, the reliability and repeatability of the haemocytometer technique are not known, as neither the range of possible cell counts obtained from a single sample with repeated counting nor the inter-observer variability has been specifically investigated. Newer haematology analysers,

▼ **99 Haemocytometer chamber. (a) A schematic drawing of one side of a haemocytometer showing the 9 large squares. (b) Photograph taken at × 20 magnification of the yellow square seen in 99a. (c) Photograph taken at × 20 magnification of part of the red square in 99a; note the unstained red blood cells seen here (arrows).**
(Photos courtesy M Camus)





▲ 100 Methylene blue technique (see *Table 26*). (a) Once the microhaematocrit tube has taken up the dye, blot the loaded end of the tube onto a gauze sponge to empty it, leaving one-third of the tube coated with new methylene blue. (b) Fill the non-coated end of the tube with undiluted CSF to about halfway (arrow shows where the column of CSF ends). (c–f) Rock the tube gently back and forth to distribute the stain evenly.

Table 26 Standard haemocytometer technique for CSF cell counts

Materials required

New methylene blue, non-anticoagulated microhaematocrit tube, gauze sponges, saline, Neubauer haemocytometer with cover slip, Petri dish, microscope

Technique

1 Draw up new methylene blue into a microhaematocrit tube by capillary action, allowing it to fill one-third of the tube

2 Blot the loaded end of the tube on a gauze sponge to empty it, leaving one-third of the tube coated with new methylene blue

3 Fill the non-coated end of the tube by capillary action with undiluted CSF to about halfway

4 Rock the tube back and forth gently to distribute the stain

5 Incubate the sample in the dye for 1–5 minutes prior to loading the haemocytometer

6 Fill both chambers of the haemocytometer with CSF

7 Allow the cells to settle by placing the haemocytometer in a humidified Petri dish (a wet gauze included inside a closed Petri dish will suffice) for 5–15 minutes prior to counting

8a Examine using the 40x objective lens; count the RBCs and WBCs separately in all nine squares on the haemocytometer (**99**) and multiply by 1.1 to obtain the number of RBCs and WBCs per microlitre. Do this in both chambers and average the two results

8b Alternatively, count the RBCs and WBCs separately within five squares (the four corner squares and the centre square) in each chamber or side, for a total of ten squares counted (**99**). Add up the number of cells in each chamber to obtain the number of RBCs and WBCs per microlitre.

(From Fry MM, Vernau W, Kass PH *et al.* (2006) Effects of time, initial composition, and stabilizing agents on the results of canine cerebrospinal fluid analysis. *Vet Clin Pathol* **35**:72–77.)

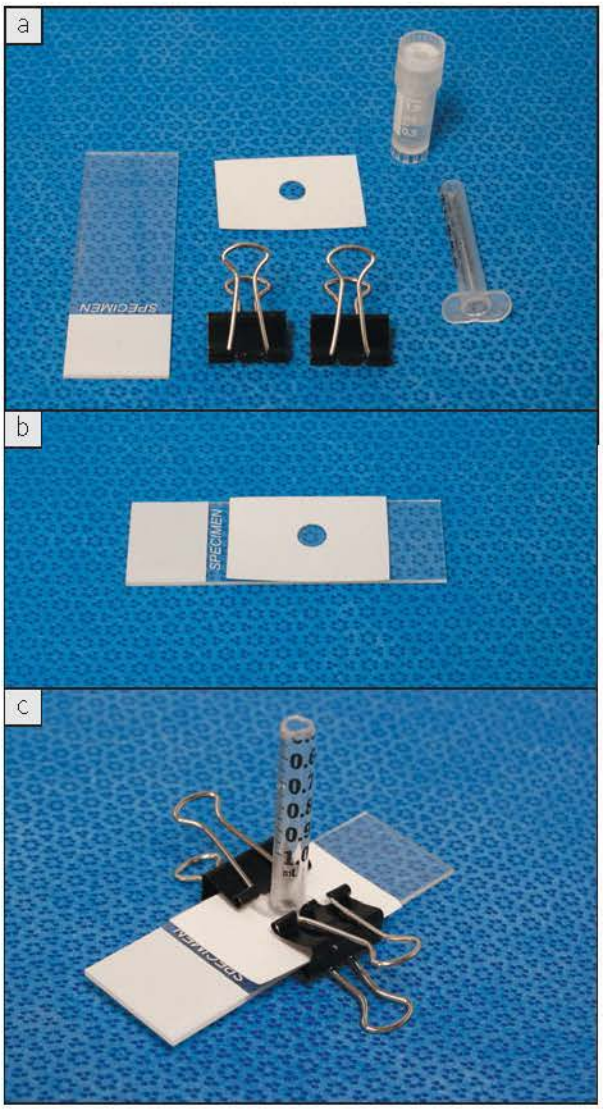
Table 27 Creation of a sedimentation technique for cytological analysis of CSF

Materials required

Standard hole puncher, two binder-type clips, filter paper, glass microscope slide, 1 ml syringe (plunger removed, cut in half) (**101**)

Technique

1. Punch a hole in the middle of the filter paper and place it on the glass slide
2. Centre the flanged end of the syringe over the hole in the filter paper
3. Clamp the flanges of the syringe barrel onto the microscope slide using the clips
4. Load 0.25–0.5 ml of CSF into the open end of the barrel
5. Allow the fluid to diffuse for 30 minutes
6. Air dry the slide (do not heat fix)
7. Send the slide to a commercial laboratory or stain with Romanowsky-type stain (such as Wright–Giemsa) for in-house examination



▶ **101 Sedimentation chamber preparation.** **(a) The materials required for sedimentation include two binder-type clips, filter paper, a glass microscope slide and a 1 ml syringe (plunger removed and cut in half). (b) Punch a hole in the middle of the filter paper and place it on the glass slide. (c) Centre the flanged end of the syringe over the hole in the filter paper, then clamp the flanges of the syringe barrel onto the microscope slide using the clips.**

such as the Advia 2120 (Siemens Medical Solutions) and Cell-Dyn 4000 (Abbott Diagnostics Division), are currently being investigated for their ability to count and differentiate the low numbers of cells in CSF. Their results correlate well in most respects with manual techniques and are less labour intensive.

Cytological analysis

Every sample of CSF that is collected should be evaluated cytologically, regardless of the TNCC, as a significant percentage of samples with normal cell counts have abnormalities in cell distribution, type or morphology. Due to the relatively low numbers of leucocytes in CSF, cells must be concentrated in order to make slides for microscopic examination. Commercial laboratories use cytocentrifugation to concentrate cells, which requires expensive equipment. Sedimentation techniques are an inexpensive way to prepare slides with good cell retrieval, although they do not preserve cell morphology as well as cytocentrifugation. Many techniques for creating a sedimentation chamber have been described; one is outlined in *Table 27* (**101**).

NORMAL CEREBROSPINAL FLUID AND IATROGENIC ALTERATIONS

Normal findings

See *Table 24* for normal findings of CSF analysis, bearing in mind that reference intervals, especially for protein concentration, often vary among laboratories.

Other cells that may be observed in normal CSF include elements of the CNS such as ependymal lining cells, choroid plexus cells, meningeal lining cells and, rarely, neurons themselves. Haematopoietic cells can occasionally be present after performing a lumbar puncture. These are probably collected from the bone marrow as the needle is advanced along the vertebra and are not a significant finding. Squamous epithelial cells can also be seen as a contaminant from the skin.

Effects of blood contamination

CSF normally does not contain erythrocytes; however, its collection, especially from the lumbar site, commonly results in contamination of the sample with peripheral blood. This may result in grossly red-tinged fluid that clears on centrifugation. Other indicators of pathological haemorrhage are discussed below (see Interpretation of abnormal CSF results, p. 130).

Contamination with peripheral blood inevitably affects the quantitative CSF analysis by increasing the erythrocyte count, TNCC and TP concentration. Although various ratios have been proposed to account for the extra leucocytes and protein in the CSF contributed by iatrogenic haemorrhage, one study has shown these to be unreliable. Typically, no leucocytes and little to no protein will accompany the many thousands of RBCs resulting from iatrogenic haemorrhage. However, when the haemorrhage contributes erythrocytes in excess of 10,000/µl, these values may be altered and it is preferable to repeat the procedure. The tap can be repeated in 24 hours to obtain a new sample.

Recently, the effect of blood contamination on CSF samples with a normal TNCC (<5 cells/µl) was studied. Blood contamination (>500 RBCs/µl) was found to increase significantly the percentage of neutrophils, the TP concentration and the presence of eosinophils. It did not, however, affect the presence of activated macrophages or reactive lymphocytes, suggesting that the presence of these cells may be a more specific indicator of neurological disease in patients with a normal TNCC and blood contamination.

Effects of recent myelographic study

Interpretation of CSF analysis can be challenging when CSF is collected following the injection of intrathecal contrast for a myelogram, as the presence of the contrast material itself in the subarachnoid space causes a mild aseptic meningitis. Metrizamide has been shown to cause a rapid rise and decline in the TNCC count over 72 hours following myelography, with a large range of peak TNCCs among dogs (from normal to >140 cells/µl) that probably is a reflection of individual variability in the reaction to the agent. A study comparing the effects of iopamidol and metrizamide myelography at 90 minutes post myelogram found that both agents caused leptomeningeal irritation, resulting in a mild neutrophilic/mixed pleocytosis (median leucocyte count following iopamidol injection: 12 cells/µl) and little change in TP concentration.

Table 28 **Gross appearance of CSF**

	CHANGE	POTENTIAL CAUSES
Colour	Pink or red	Iatrogenic contamination; recent subarachnoid haemorrhage (within a few hours)
	Yellow or yellow-orange (xanthochromia)	Erythrocyte breakdown products from previous haemorrhage (within past 8–14 days); bilirubin from hyperbilirubinaemia or disrupted blood–brain barrier; markedly increased TP
Clarity	Turbid	TNCC >500 cells/μl

INTERPRETATION OF ABNORMAL CSF RESULTS

Abnormal gross appearance

See *Table 28*.

Increased total protein

Elevation in CSF protein concentration is a sensitive indicator of CNS disease, but it is the least specific change observed on CSF analysis and accompanies increased leucocyte counts virtually every time that abnormality is seen. The concentration of protein in the CSF can be increased due to abnormalities in the blood–brain barrier or to intrathecal globulin production. Albuminocytological dissociation is the term used to describe an elevation in the microprotein concentration with a normal leucocyte count. This occurs with diseases that cause intrathecal production of protein, obstruct the flow of CSF and allow protein accumulation, or disturb the blood–brain barrier enough to allow protein from peripheral blood to enter the CNS. These conditions tend to be non-inflammatory in aetiology, though there are exceptions to this generalization. (See *Table 29* for potential causes of albuminocytological dissociation.)

Increased total nucleated cell count

(See *Table 30* for a summary of the expected ranges of TNCC with various categories of disease.) Note that there is significant overlap and that the differential cell count must be considered in order to maximize the diagnostic yield of CSF analysis. Abnormalities in the differential cell count are described individually below, and potential causes are listed in *Table 31*.

Table 29 **Causes of CSF albuminocytological dissociation**

- Intervertebral disc disease or other extradural compressive lesion*
- Trauma*
- Degenerative myelopathy (normal to mildly increased protein)
- Ischaemic injury (such as fibrocartilaginous embolism) causing infarction*
- Vasculitis or vascular lesion with haemorrhage
- Intrathecal globulin production caused by infection (e.g. canine distemper, FIP)
- Neoplasia* (due to intrathecal globulin production, interference with blood vessel integrity or necrosis of the adjacent parenchyma)
- Recent seizure activity
- Polyradiculoneuritis
- Inflammatory CNS disease following corticosteroid treatment (which decreases the TNCC)*

* Indicates conditions in which the neutrophil percentage of the differential cell count may be increased.

Table 30 **Differential diagnoses based on total nucleated cell count alone**

5–25 cells/μl	Vascular*, trauma*, neoplasia, IVDD*, syringomyelia, recent seizure activity*
25–50 cells/μl	Trauma*, neoplasia, +/- vascular*, IVDD*, inflammatory
>50 cells/μl	Inflammatory (infectious or sterile), less commonly IVDD*, trauma*

* Pleocytosis should resolve by 2–7 days following insult in these conditions.

IVDD = intervertebral disc disease.

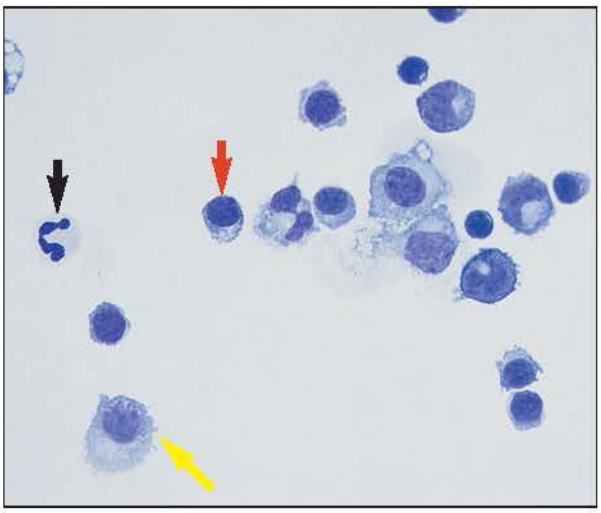
Table 31 Disease differentials to consider based on the cytological interpretation of the CSF

Mixed pleocytosis	Lymphocytic pleocytosis	Neutrophilic pleocytosis	Eosinophilic pleocytosis
• GME • Infectious diseases (protozoal, rickettsial, less commonly fungal) • Neoplasia • Trauma • Intervertebral disc disease • Fibrocartilaginous embolism	• Viral encephalitides (other than FIP) • NME/NLE • GME • Neoplasia, especially lymphoma • Protozoal or fungal infections • Infarction • Intervertebral disc disease • Less commonly, other infectious diseases (*Ehrlichia canis* or bacterial infection, especially following antibiotic therapy), SRMA, parasitic migration or feline polioencephalomyelitis	• Bacterial meningoencephalomyelitis • SRMA (often >80% neutrophils) • FIP (can be >70% neutrophils) • Neoplasia (can be >90% neutrophils) • Fungal infection • Infarction • Protozoal infections • Trauma/haemorrhage • Acute intervertebral disc disease • Rarely, GME (>60% neutrophils have been reported)	• EME (can be >90% eosinophils) • Cryptococcosis (up to 80% eosinophils reported) • Protozoal infections • Parasitic migration (*Baylisascaris, Cuterebra, Angiostrongylus*) • Intervertebral disc disease • Uncommonly, GME

GME = granulomatous meningoencephatitis; FIP = feline infectious peritonitis; NME = necrotizing meningoencephalitis; NLE = necrotizing leucoencephalitis; SRMA = steroid responsive meningitis–arteritis; EME = eosinophilic meningoencephalomyelitis.

In a **mixed pleocytosis**, no single cell type predominates (**102**); it contains a mixture of mostly lymphocytes and large mononuclear cells, with smaller numbers of macrophages, neutrophils and, occasionally, plasma cells and eosinophils. Numerous conditions can be associated with a mixed pleocytosis, the most notable being GME, in which the cell counts are often markedly elevated (average 800 cells/µl in one study).

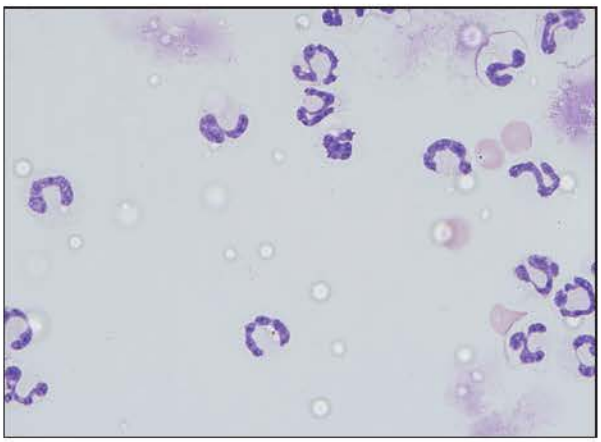
A **lymphocytic pleocytosis** is characterized by an elevated TNCC with >50% lymphocytes. It is the most common form of **mononuclear pleocytosis** and usually consists of a majority of small, mature lymphocytes, with smaller numbers of reactive lymphocytes and larger monocytoid cells. It occurs commonly in cases of viral disease, notably canine distemper virus, in which the cell count is typically <50 cells/µl, but it can also be associated with other chronic CNS infections. Necrotizing meningoencephalitis (NME) and necrotizing leucoencephalitis (NLE) cause a strongly lymphocytic (>80%) pleocytosis with a moderately to markedly elevated cell count. Rather than being mixed, the pleocytosis in GME frequently has a predominance of lymphoplasmacytic cells.



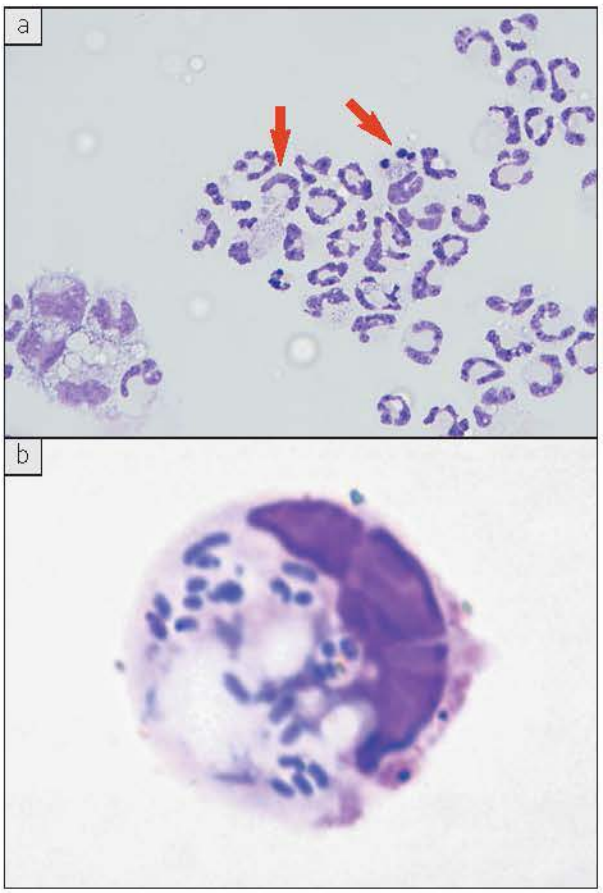
▲ **102 Mixed pleocytosis. Small lymphocytes (red arrow), monocytes (yellow arrow) and a neutrophil (black arrow) can be seen. (Wright–Giemsa; × 100 objective) (Photo courtesy M Camus and E Cienava)**

A **neutrophilic pleocytosis** is defined as an elevated TNCC with a predominance of neutrophils (**103**). However, diseases known to cause neutrophilic pleocytosis should be considered when neutrophils constitute >2% of the nucleated cells whether or not neutrophils are the predominant cell type. In general, when there is a very high nucleated cell count and neutrophils are the predominant cell type present, suppurative inflammatory processes (e.g. steroid responsive meningitis–arteritis [SRMA], bacterial or fungal meningoencephalitis/meningoencephalomyelitis) must be considered. A mild to moderate neutrophilic pleocytosis can be associated with acute inflammatory disorders, including trauma, post-myelographic aseptic meningitis, encephalitis of unknown aetiology, haemorrhage, necrosis, infarction and neoplasia. Historically, meningiomas (especially those in the caudal fossa) have been associated with a neutrophilic pleocytosis, but various other tumour types can cause this change. Degenerate neutrophils may or may not be observed in cases of bacterial infection (**104**).

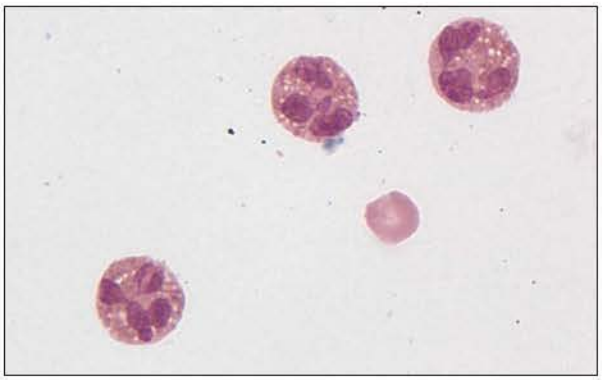
While the presence of eosinophils in the CSF in the absence of significant peripheral blood contamination is not normal, it is often a non-specific change. A differential cell count with >10–20% eosinophils is considered an **eosinophilic pleocytosis** (**105**). This is an uncommon finding and has been associated with an eosinophilic meningoencephalomyelitis (EME) of unknown aetiology in both dogs and cats, aberrant parasitic migration, various infectious agents (particularly protozoa and fungi) and, rarely, intervertebral disc disease (IVDD). The TNCC can be markedly elevated (>1000 cells/μl) in cases of EME, cryptococcosis and *Baylisascaris* migration.



▲ **103** Neutrophilic pleocytosis. (Wright–Giemsa; × 40 objective) (Photo courtesy R Di Terlizzi)



▶ **104** (a) Degenerative neutrophilic pleocytosis in CSF, with intracytoplasmic organisms evident (arrows). (× 40; Photo courtesy M Camus and E Cienava); (b) Atlanto-occipital CSF from a dog with bacterial meningitis. The cytocentrifuge sample revealed a degenerate neutrophil. Associated with the karyolitic neutrophil, small rod-shaped bacteria are present intracellularly and often within intracytoplasmic phagosomes. (Wright–Giemsa; × 100 objective) (Photo courtesy R Di Terlizzi)

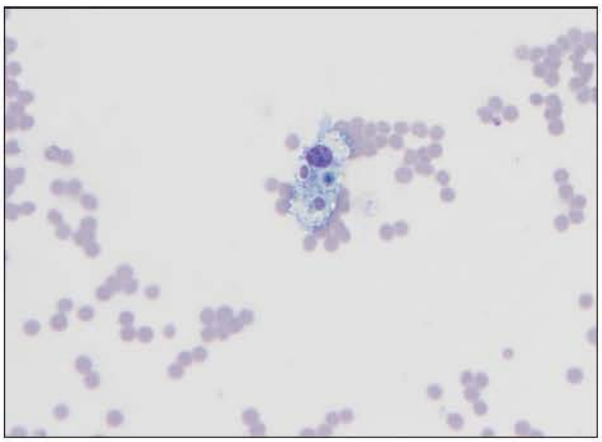


▲ 105 Eosinophilic pleocytosis. Three eosinophils and one erythrocyte are present in this image from a dog with immune-mediated eosinophilic meningitis. (Wright–Giemsa; × 40 objective) (Photo courtesy R Di Terlizzi)

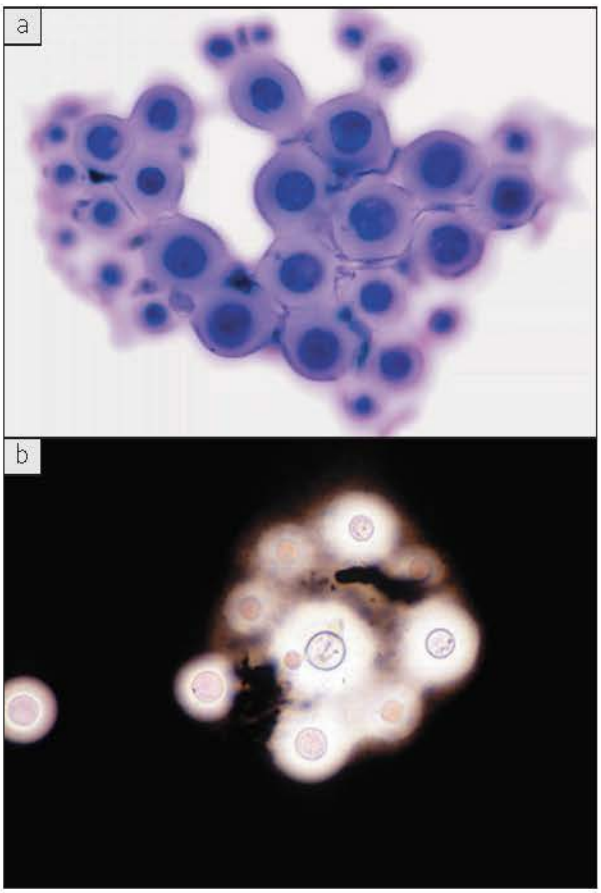
Other cytologic abnormalities

Macrophages can be found in CSF and represent a non-specific reaction to inflammation, haemorrhage or degeneration. They may be vacuolated and may contain phagocytosed cells or infectious agents. The presence of erythrophagocytosis indicates pathological rather than iatrogenic haemorrhage (**106**). Plasma cells can also represent a non-specific inflammatory response. They are most often seen in cases of GME, but can also be present in NME and various infectious diseases.

Infectious agents themselves can occasionally be visualized on a cytospin preparation. These include bacteria, fungal elements, *Ehrlichia* morulae, protozoa and distemper inclusion bodies. *Cryptococcus*, being a generally surface-oriented fungus, has reportedly been observed in the CSF in the majority of cases of CNS infection; if suspected, India ink preparations aid in the visualization of the organism (**107**).



▲ 106 Erythrophagocytosis. The cell in the centre of the field contains red blood cells. (Wright–Giemsa; × 40 objective) (Photo courtesy M Camus and E Cienava)

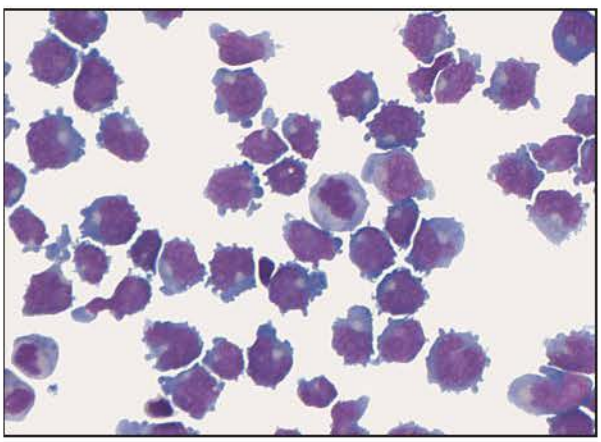


▶ 107 (a) This sample contains a cluster of basophilic-staining extracellular yeast forms consistent with *Cryptococcus* spp. (Wright–Giemsa; × 100 objective) (b) Same sample stained with India ink. (Photos courtesy R Di Terlizzi)

It is uncommon to find neoplastic cells in the CSF. Neoplasia reported to exfoliate into the CSF includes lymphoma (**108**), choroid plexus carcinoma and malignant histiocytosis. Neural elements can also occasionally be seen in the CSF. Myelin may be seen (either phagocytosed inside macrophages or as free myelin, also called myelin fragments) in cases of myelomalacia or demyelinating conditions such as degenerative myelopathy. In cases of lysosomal storage diseases, large inclusions can be found in CSF mononuclear cells; the appearance of the inclusions depends on the accumulated metabolic product.

ADDITIONAL TESTS

An increasing number of supplemental tests is available to perform on CSF. This includes tests for CSF glucose and globulin levels, tests for specific infectious diseases and newly developed tests whose clinical usefulness is still to be determined.



▲ **108** **Atlanto-occipital CSF from a 9-year-old Labrador Retriever. Medium to large lymphocytes can be seen with immature chromatin, prominent nucleoli and basophilic, often vacuolated, cytoplasm. (Wright–Giemsa; ×100) (Photo courtesy R Di Terlizzi)**

Glucose and protein assays

Depending on the reference laboratory, CSF glucose concentration may be measured as part of a routine analysis; it can also be measured using a standard glucometer. The concentration of glucose in the CSF depends in large part on the serum glucose concentration, so this should be measured simultaneously. Glucose levels in the CSF should be between 60% and 80% of the serum glucose, although there is an approximately 1–2 hour delay before acute changes in serum glucose are reflected in the CSF. Decreased glucose concentration in the CSF (hypoglycorrhachia) is observed most commonly in cases of bacterial meningitis.

Increases in CSF protein result from increased permeability of the blood–brain barrier, intrathecal globulin production, or both. To discern the mechanism, the protein in CSF can be further analysed for the albumin quotient, which detects disruptions in the blood–brain barrier, and for increased globulins, which indicates intrathecal production. The percentages of albumin and alpha-, beta- and gamma-immunoglobulins (Ig) in CSF can be measured by protein electrophoresis. These techniques and the interpretation of the results are discussed in detail elsewhere. Enzyme-linked immunosorbent assay (ELISA) tests have also been developed to quantify the IgG, IgA and IgM content of the gammaglobulin fraction within the CSF, and accumulation of these substances has been associated with inflammatory CNS conditions. Of particular interest is that CSF levels of IgA are highest in patients with SRMA. These levels remain elevated during treatment and in the event of remission. While not entirely specific, the combination of elevated CSF and serum IgA is a very sensitive indicator of SRMA and may be a useful diagnostic test if clinical suspicion of the disease is high, but the standard CSF analysis is normal.

Infectious disease testing

Screening for infectious diseases is often a critical step in the assessment of neurological disease, especially since the clinician frequently has to decide in the face of an inflammatory process between treating a patient with an immunosuppressive or an antimicrobial drug regimen. Based on the signalment, history, geographic location, physical and neurological examination findings and results of other diagnostic tests, a list of possible infectious diseases can be made and the appropriate tests selected (see Chapter 19).

Table 32 **Infectious disease testing on CSF samples**

INFECTIOUS AGENT	ANTIBODY TITRES	ANTIGEN TITRES	PCR
Canine distemper virus	+		+
Feline infectious peritonitis	+		+ (low sensitivity)
Brucella canis	+	+	+
Ehrlichia canis	+		+
Rickettsia rickettsii	+		+
Toxoplasma	+		+
Neospora	+		+
Cryptococcus		+ (highly sensitive and specific)	
Blastomyces	+		
Aspergillus	+ (false negatives possible; many dogs are seropositive)		
Coccidiomyces	+ (low sensitivity)		
Histoplasma	+ (low sensitivity and specificity)		

In general, aerobic and anaerobic culture of CSF is performed if there is a suspicion of bacterial meningoencephalomyelitis; however, this is an insensitive test, as false-negative results occur in over 70% of cases. Fungal culture (especially for *Cryptococcus*) and virus isolation can also be performed on CSF, but have largely been replaced by antigen or antibody titres and polymerase chain reaction (PCR) testing. CSF antibody titres are thought to be more reliable than serum titres for diagnosing infectious disease within the CNS. To distinguish true intrathecal antibody production from contamination of the CSF with antibodies from the peripheral blood that may be present in the event of a compromised blood–brain barrier, the antibody coefficient can be calculated. This allows for the presence of blood-derived antibodies by normalizing the titre for the disease under investigation against the titre for a disease that does not affect the CNS (e.g. canine adenovirus or parvovirus).

$$\text{Antibody coefficient} = \frac{\text{disease-in-question antibody in CSF}}{\text{disease-in-question antibody in serum}} \times \frac{\text{non-CNS disease antibody in serum}}{\text{non-CNS disease antibody in CSF}}$$

Coefficients >1 provide evidence for intrathecal production of antibodies against the disease in question. PCR assays have been developed for many infectious agents affecting the CNS, and while these are valuable tests, they are neither 100% sensitive nor specific and should be used in combination with other diagnostic tests when possible. (See *Table 32* for currently available diagnostic tests that can be performed on CSF for the detection of common CNS pathogens.)

Table 33 **CSF analytes of possible future clinical significance**

CSF ANALYTE	RELEVANCE
Myelin basic protein	Used as a marker of demyelination; may be useful in antemortem diagnosis of degenerative myelopathy
Glutamate	Elevated in dogs with acute and chronic spinal cord compression caused by IVDD; excitotoxicity may play a role in secondary spinal cord injury and therefore become a therapeutic target. Elevated in dogs with idiopathic epilepsy; may indicate that chronic overexcitation caused by elevated glutamate levels contributes to the pathogenesis of idiopathic epilepsy
Matrix metalloproteinase-9	Elevated during the first 24 hours following acute spinal cord injury caused by IVDD and varies directly with severity of neurological deficits; may have prognostic significance or present a therapeutic target
Beta-2-microglobulins	Sensitive indicator of inflammation in IVDD; may be useful as a prognostic marker. Markedly elevated in dogs with inflammatory CNS disease; may be useful for diagnosing the cause of inflammation or monitor disease progression

IVDD = intervertebral disc disease; CNS = central nervous system.

Assays under investigation

Many CSF analytes are being studied both for their potential to expand our understanding of the pathogenesis of various diseases and injuries and for their potential clinical usefulness. Several of these analytes and their area of relevance are listed in *Table 33*. One test that has recently been validated and is commercially available is the PCR for antigen receptor rearrangement (PARR) for the detection of lymphoid neoplasia. The goal of this test is to distinguish a clonal neoplastic population of lymphocytes from a genetically diverse population (as could occur with lymphoid hyperplasia or response to an antigenic stimulus). PCR primers direct replication of surface portions of the T-cell and B-cell receptors on lymphocytes. The test can be performed on a variety of tissue samples, including CSF; however, its sensitivity depends on the nature and cellularity of the tissue. When performed on tissues such as bone marrow, cavity fluids, peripheral blood and lymph node, the reported sensitivity is 75% for dogs and 65% for cats, and the reported specificity is 94%. However, the sensitivity and specificity for this test when performed on CSF are currently unknown and may be lower than for other tissues because of the typically low cellularity of CSF. An inadequate number of cells in a sample may prevent a clonal arrangement from being detected, leading to a false-negative result, and an insufficient number of lymphocytes may make a heterogeneous population appear clonal, leading to a false-positive result. It is also not known how or whether the TNCC of a CSF sample affects the test's reliability. Further research is needed to understand the utility of this test in detecting lymphoproliferative diseases in the CNS.

PART 2

DECISION MAKING

CHAPTER 6 Obtundation, stupor and coma

CHAPTER 7 Seizures

CHAPTER 8 Exercise-associated weakness and collapse

CHAPTER 9 Ataxia

CHAPTER 10 Acute paresis and paralysis

CHAPTER 11 Spinal pain

CHAPTER 12 Acute blindness

CHAPTER 13 Acute tremors and involuntary movements

CHAPTER 14 Head tilt and nystagmus

CHAPTER 15 Acute disorders of the head and face

CHAPTER 16 Monoparesis and neurological causes of lameness

OBTUNDATION, STUPOR AND COMA

Peter Dickinson

INTRODUCTION

Assessment of the level of consciousness of an animal is one of the most important and, often, most neglected, components of the neurological examination. Alterations in consciousness are usually reflective of diseases, or exposure to substances, that result in dysfunction of the brainstem and/or the cerebrum. Alterations may be acute or chronic in nature and may vary from subjectively subtle alterations to profound dysfunction. Alterations may also result in changes in quality of mentation (e.g. inappropriate behaviour) as well as changes in absolute levels. Assessment of consciousness is based on an animal's responses, either appropriate or inappropriate to its environment, and stimuli, both normal and abnormal, within that environment. As such, familiarity with the range of normal responses of cats versus dogs, young animals versus old animals and highly active breeds such as terriers versus less active giant breeds is important in the assessment of mentation.

Inappropriate behaviour or a decreased level of consciousness is a strong indicator of intracranial disease; however, severe systemic disease, such as cardiorespiratory insufficiency, metabolic disease and exposure to exogenous toxins, can also result in secondary effects that produce similar if not identical clinical signs. When combined with other findings of the neurological examination, appropriate localization of neurological disease and formation of an appropriate differential list and diagnostic plan become possible (*Table 34*).

Table 34 Differential diagnoses for obtundation, stupor and coma

DISEASE MECHANISM	DOGS	CATS
Vascular	Brain infarct	Brain infarct
	Brain haemorrhage	Brain haemorrhage
	Hypertension	Hypertension
		Feline ischaemic encephalopathy (*Cuterebra* migration)
Inflammatory/infectious	Infectious encephalitis (distemper, *Toxoplasma, Neospora*, fungal, bacterial, rickettsial, rabies)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, *Cryptococcus*, rabies)*
	Meningoencephalitis of unknown aetiology (GME, necrotizing)*	Meningoencephalitis of unknown aetiology (presumed immune mediated); rare
Trauma	Head trauma*	Head trauma*
Toxic	Anticoagulants (secondary haemorrhage)	Anticoagulants (secondary haemorrhage)
	Ivermectin	Ivermectin
	Hexachlorophene	Hexachlorophene

* Common cause

(Continued)

Table 34 **Differential diagnoses for obtundation, stupor and coma** (*continued*)

DISEASE MECHANISM	DOGS	CATS
Toxic	Barbiturates	Barbiturates
	Ethylene glycol*	Ethylene glycol
	Lead	Lead
	Metaldehyde	Metaldehyde
	Theobromine (chocolate)*	Theobromine (chocolate)
	Opioids	Opioids
	Phenothiazine tranquilizers	Phenothiazine tranquilizers
	Recreational drugs	Recreational drugs
	Anticonvulsants	Anticonvulsants
Anomalous	Hydrocephalus*	Hydrocephalus
Metabolic	Hypoxia/ischaemia*	Hypoxia/ischaemia*
	Syncope (transient)	Syncope (transient)
	Excitotoxicity (post ictal)	Excitotoxicity (post ictal)
	Hepatic encephalopathy*	Hepatic encephalopathy
	Uraemia	Uraemia
	Hyperthermia	Hyperthermia
	Osmotic abnormalities (Na^+ imbalance)	Osmotic abnormalities (water intoxication)
	Hypoglycaemia*	Hypoglycaemia
	Ketoacidosis*	Ketoacidosis
	Hypoadrenocortical crisis	
	Hypothyroidism	
Idiopathic	Narcolepsy	
Neoplastic	Primary or metastatic brain tumour*	Primary or metastatic brain tumour*
Nutritional	Thiamine deficiency	Thiamine deficiency

* Common cause

NEUROANATOMICAL BASIS

The reticular formation is composed of a network of both ascending and descending neurons and forms both the most primitive, and the most extensive, component of the neuraxis in all mammals. On an evolutionary basis, it corresponds to the basic nerve networks of invertebrates and primitive vertebrates. The ascending component of the reticular system forms a diffuse midline system and receives input from all sensory modalities (except muscle and joint proprioception) at the level of both the spinal cord and the brainstem, and projects this information diffusely to the cerebral cortex via the thalamus (**109**). The ascending reticular formation arouses all areas of the cerebral cortex, resulting in a normal level of consciousness. Because of this the ascending reticular formation is referred to as the reticular activating system (RAS). The true seat of consciousness is the cerebral cortex; however, the RAS is critical for adjusting the level of cerebral activity, and damage to either area or interruption of the communication between the RAS and the cerebrum will result in abnormal levels of mentation.

The rostral pons and caudal midbrain in the brainstem are particularly important areas in their contribution to the RAS and are important in mediating the effects of CNS depressants and stimulants.

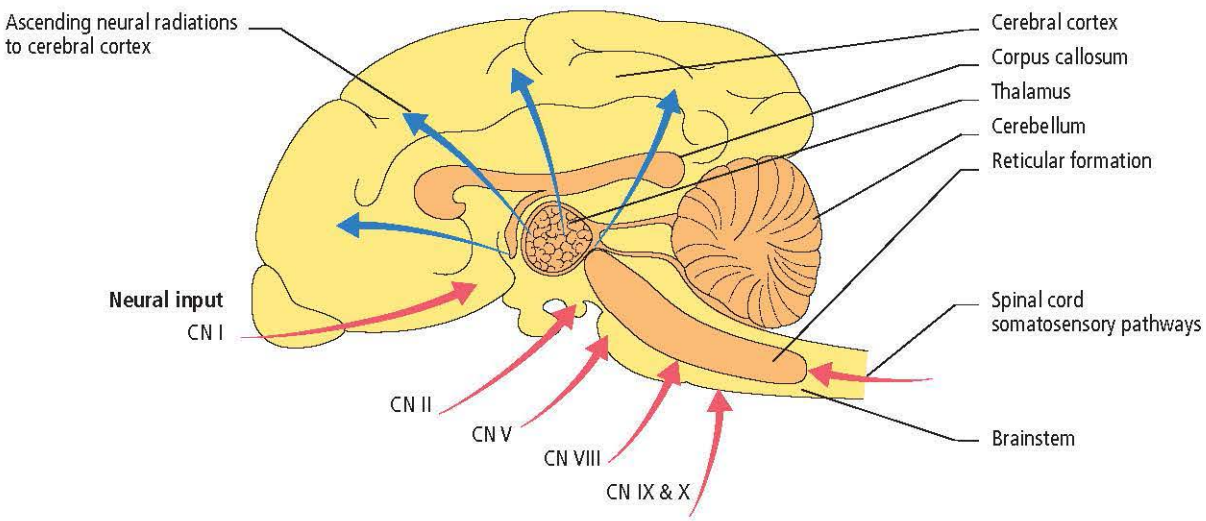
Sleep, which represents a physiologically normal decrease in the level of consciousness, is a complex process involving neuronal systems in the medulla, pons and midbrain that under normal circumstances have generally inhibitory actions on the RAS. Normal sleep can be characterized, in some phases, by the presence of synchronous neuronal activity of cortical neurons on an electroencephalogram (EEG). Input from the RAS typically disrupts this synchrony (i.e. desynchronizes the cortex), resulting in arousal.

NEUROLOGICAL EVALUATION

The first component of a complete neurological examination consists of general observations, including assessment of the level of mentation and behaviour exhibited by the animal. If possible, an animal should be allowed to move around the examination room freely so that its response to both the local environment and the people present can be assessed. This may be accomplished while the examiner is obtaining the pertinent history and presenting problems from the owner.

Mental status may be categorized as:

- Bright and alert (normal).
- Obtunded: conscious, but with reduced activity and responsiveness to environmental stimuli. There may be an increased tendency to sleep when not stimulated. This is a non-specific finding, as it may result from systemic disease as well as CNS disease.
- Stuporous: sleeps or is unresponsive to innocuous stimuli such as noise, but will respond to painful stimuli. Both obtundation and stupor may be further classified subjectively as mild, moderate or severe. This results from a disease diffusely affecting both hemispheres and/or the brainstem.
- Comatose: state of unconsciousness. Cannot be aroused even with painful stimuli, although some simple reflexes may be present. This also results from a disease diffusely affecting both hemispheres and/or the brainstem.



▼ 109 **Schematic representation of the ascending reticular activating system (ARAS). The spinal cord somatosensory pathways, as well as the sensory component of cranial nerves I, II, V, VIII, IX and X, project onto the brainstem reticular formation. The latter, in turn, diffusely activates the cerebral cortex to maintain a state of consciousness.**

Terms such as depression and delirium should generally be avoided when describing animals with altered mentation, since their definition requires an assessment of cognition and emotion.

Additional observations that can be made during this period include inappropriate behaviour (aggression, fearlessness, ignoring specific stimuli), compulsive behaviour, pacing, circling and head pressing (**110**, **111**). Any or all of these findings are suggestive of intracranial disease affecting the forebrain (cerebrum and thalamus), and may be found coincidentally with a decreased level of consciousness.

Diffuse or multifocal disease of the cerebral cortex

In general, diffuse or multifocal disease of the cerebral cortex results in obtundation or stupor, although very severe disease with an acute onset may occasionally result in coma. Additional neurological deficits reflect the diffuse cortical localization and may include bilateral visual and menace deficits with normal PLRs, bilateral loss of placing reactions and seizures. Mild tetraparesis may be present; however, animals are often non ambulatory. Common causes reflect the diffuse localization and include metabolic disease, hypoxia/ischaemia (e.g. secondary to status epilepticus or hyperthermia) intoxications and any severe focal disease that results in secondary global increases in ICP (e.g. a space-occupying mass with peri-lesional oedema or hydrocephalus).

Disease restricted to one cerebral hemisphere

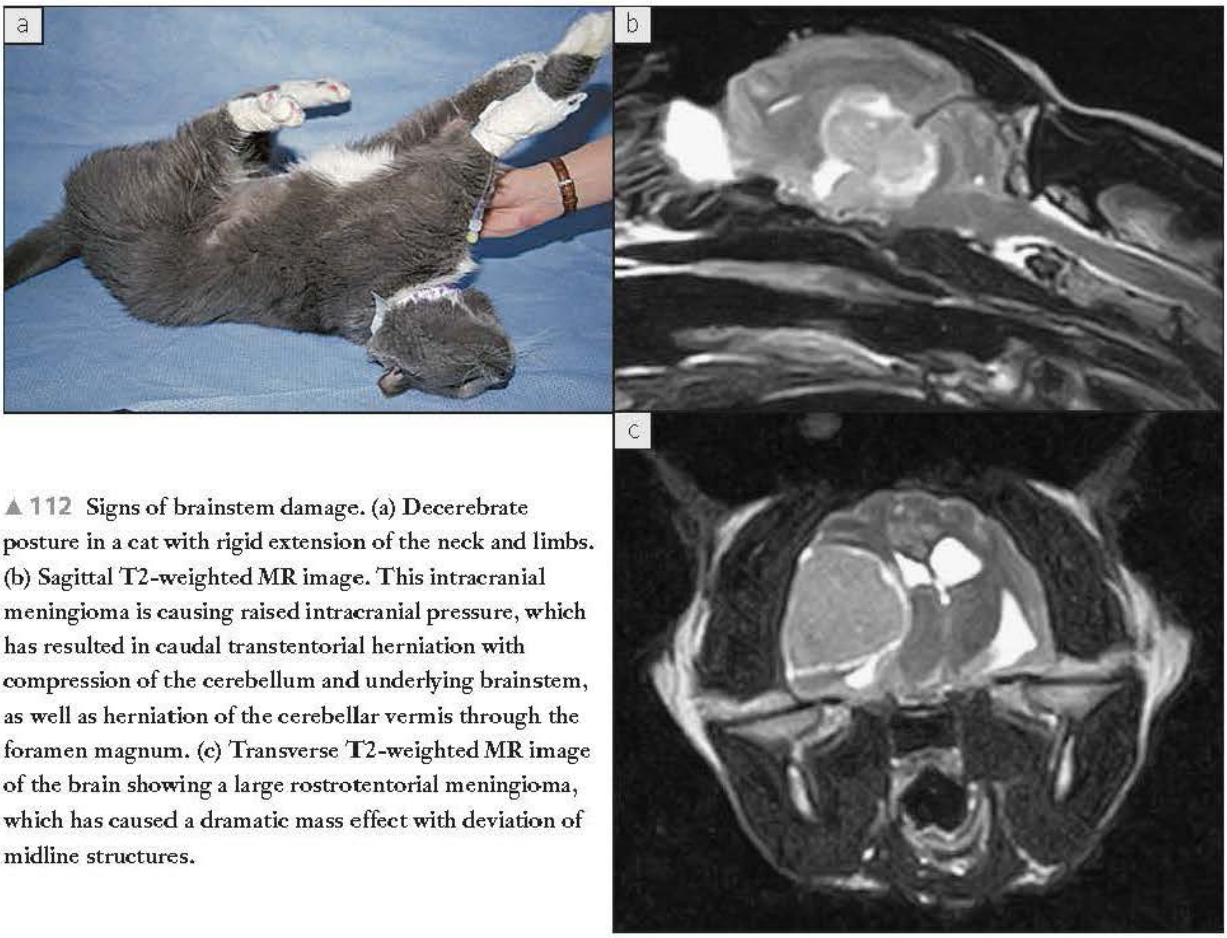
Any disease predominantly affecting one cerebral hemisphere usually results in obtundation +/- contralateral visual and menace deficits, contralateral loss of placing reactions, mild contralateral hemiparesis, circling towards the side of the lesion and seizures. The more focal localization resulting in the lateralizing signs is suggestive of less diffuse disease processes including intracranial neoplasia, trauma, focal infectious/inflammatory disease and focal vascular disease such as infarction or haemorrhage.

▼ **110** Head pressing and getting 'stuck' in corners are typical signs in animals with extensive forebrain lesions and elevated intracranial pressure.



▼ **111** A decreased gag reflex is commonly seen in severely stuporous and comatose animals and intubation to protect the airways is recommended. Intensive nursing may be required.





▲ 112 Signs of brainstem damage. (a) Decerebrate posture in a cat with rigid extension of the neck and limbs. (b) Sagittal T2-weighted MR image. This intracranial meningioma is causing raised intracranial pressure, which has resulted in caudal transtentorial herniation with compression of the cerebellum and underlying brainstem, as well as herniation of the cerebellar vermis through the foramen magnum. (c) Transverse T2-weighted MR image of the brain showing a large rostrotentorial meningioma, which has caused a dramatic mass effect with deviation of midline structures.

Disease affecting the brainstem

Brainstem disease may result in altered consciousness ranging from obtundation to coma depending on the severity of the disease. Most cases of coma result from damage to the brainstem, particularly the rostral brainstem, with disruption of the RAS or its projections to the cerebrum. Structural disease affecting the rostral brainstem will also often result in pupillary abnormalities, including anisocoria (see Chapter 15), and, as severity increases, pupils often progress from miotic to unresponsive and mydriatic. Loss of physiological nystagmus and decreased gag reflex are commonly seen; however, these may also be present with more diffuse disease, particularly when there is elevated ICP.

Brainstem lesions are more likely to result in significant paresis compared with cerebral disease, and if lesions are severe and involve the midbrain, a decerebrate posture may be seen. Decerebration typically results from functional separation of the cerebrum from the brainstem, but may occur less commonly due to diffuse destruction of the cerebrum bilaterally. Signs include coma, rigid extension of all limbs and opisthotonus (extension of the neck and spine) (**112**). Common causes of brainstem disease reflect the more focal localization and include trauma, transtentorial herniation secondary to elevated ICP, neoplasia, vascular disease and inflammatory/infectious disease.

Examination pitfalls associated with altered levels of consciousness

Assessment of altered consciousness can be a subjective process, particularly when animals are only minimally affected and are judged to be mildly or moderately obtunded. It is not always possible to determine whether an animal is truly obtunded or has an apparently altered level of consciousness due to other factors, some of which are listed below. It is important to remember that there may be primary neurological disease resulting in altered consciousness (e.g. trauma or neoplasia), systemic disease resulting in secondary alteration of neurological function (e.g. metabolic/toxic disease) and, importantly, other conditions where the outward behavioural manifestations may mimic an altered level of consciousness. There may also be a combination of these factors. Additional neurological abnormalities may help to confirm a primary neurological disease in origin; however, it is often necessary to rule out systemic disease and other potential causes of 'lethargy' rather than true obtundation. Repeating the neurological examination over a period of time in different environments will help to define the true origin of the abnormal findings.

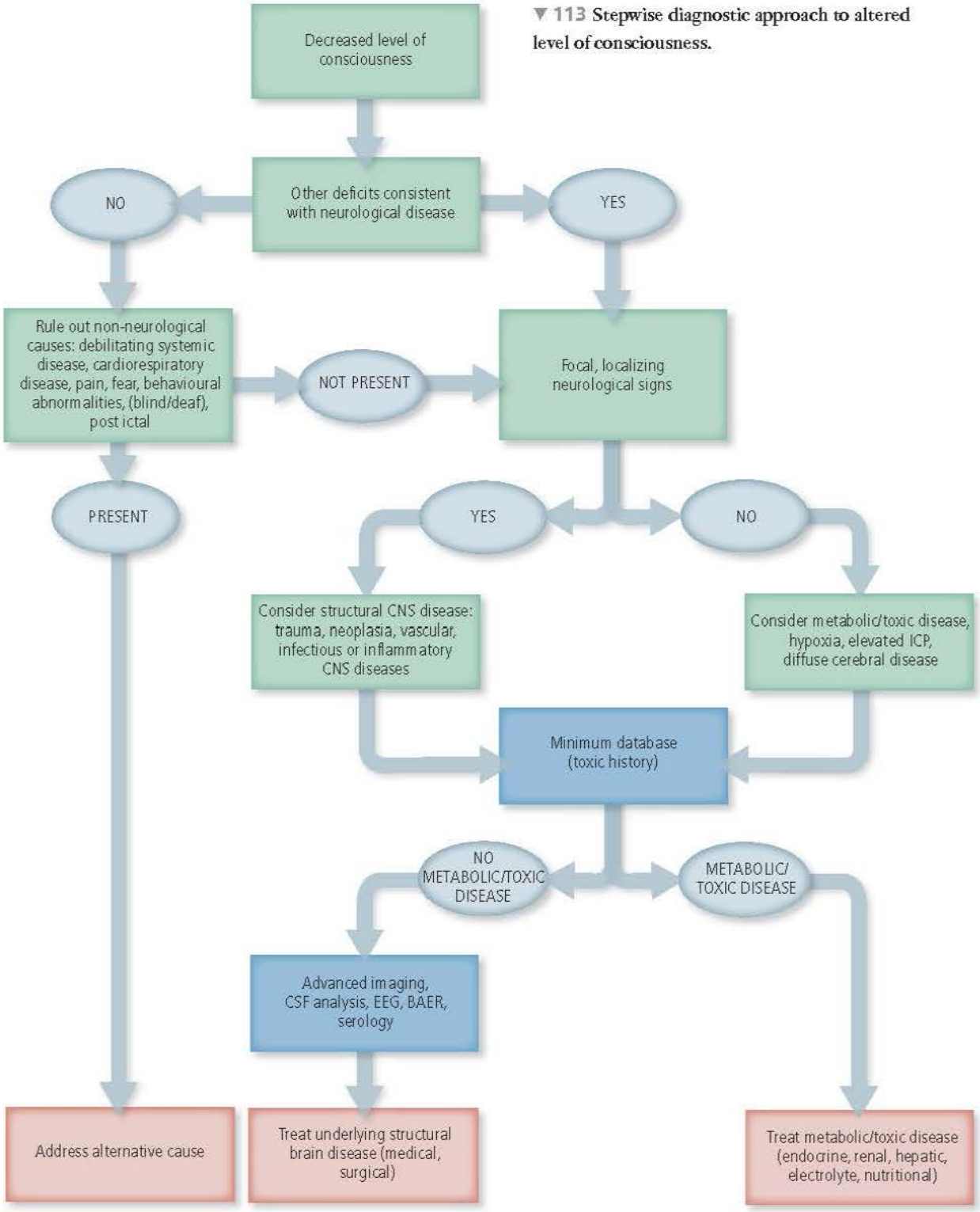
The following factors should be considered when assessing animals with apparently decreased responsiveness to external stimuli:

- Animals with debilitation due to severe systemic disease such as sepsis, uraemia, hypoglycaemia and other severe metabolic or endocrine disorders may present with lethargy rather than true decreased levels of consciousness, although concurrent secondary neurological effects are possible. Similarly, post-traumatic complications, such as hypotension, hypothermia and hypoxia, may result in apparent or true alterations in consciousness. Correcting any underlying systemic abnormalities is essential before specifically investigating primary neurological causes.
- Behaviour and mentation should be interpreted in the context of age and species-dependent normals.
- Animals with severe pain and/or fear may present for apparently altered mentation.
- Acute loss of vision and/or hearing will often result in apparently altered mentation and decreased interaction with the animal's environment.
- Post-ictal animals can exhibit a wide variety of abnormalities including altered levels of consciousness. (However, prolonged status epilepticus may result in diffuse cortical necrosis secondary to a hypermetabolic state and hypoxia.)
- Always be aware of potential exposure to medications/drugs, either prescribed or otherwise, that can have profound effects on levels of consciousness.
- Transient alterations in level of consciousness may be seen with specific conditions (e.g. narcolepsy/cataplexy) and with syncope and be associated with systemic tumours such as insulinomas and pheochromocytomas.

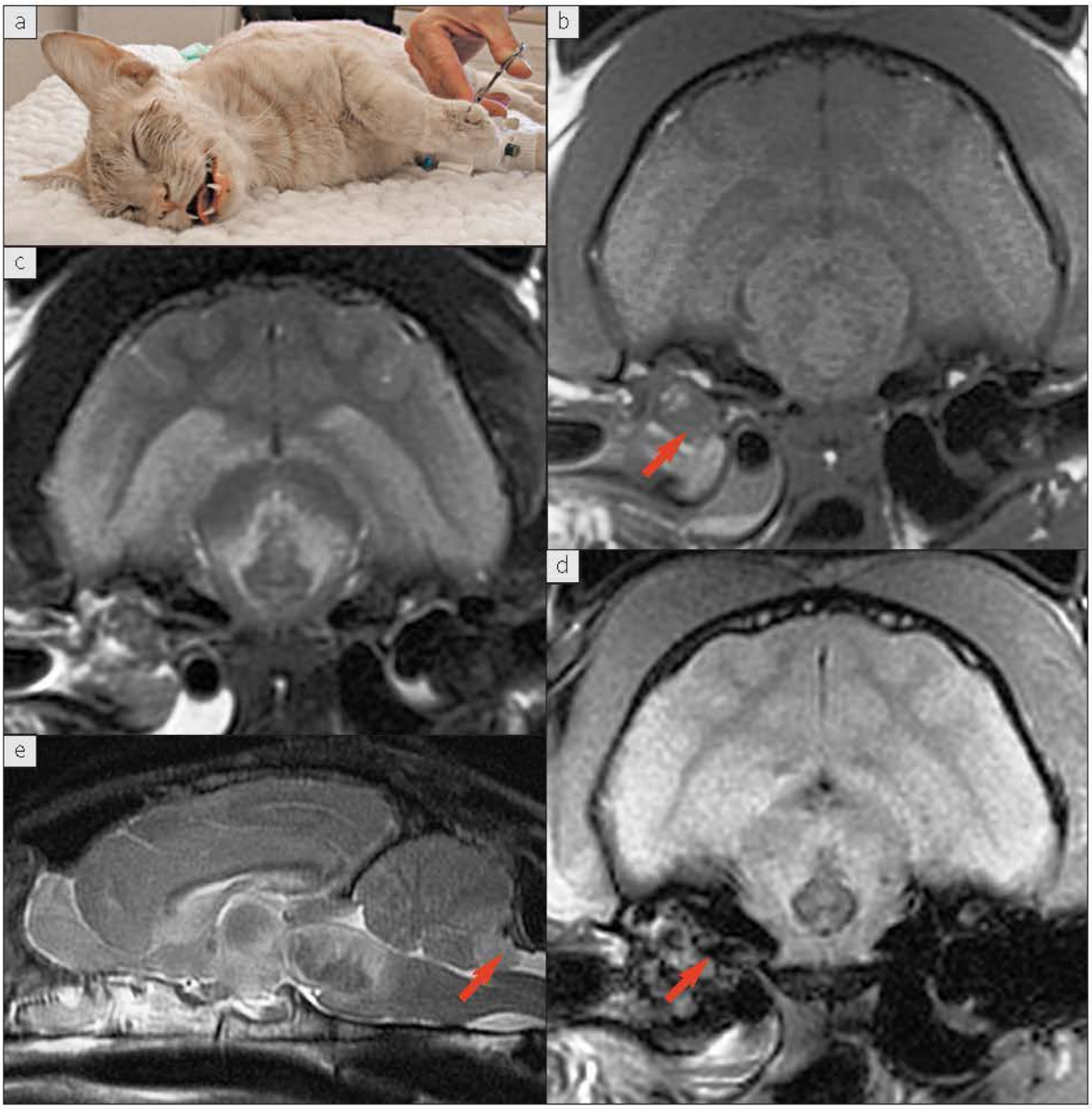
SPECIFIC DIAGNOSTIC TESTS

Systemic and metabolic diseases are a major cause of either true or apparently decreased levels of mentation in many animals. A thorough physical examination and minimum database should be done in these patients prior to pursuing specific neurodiagnostic procedures.

The choice of specific neurodiagnostic techniques depends on the most likely underlying cause and location of the lesion (**113**). Although some diagnostic techniques, such as advanced imaging, may be indicated to investigate potential intracranial disease, the overall medical condition of the patient must be assessed and the risks and benefits calculated, particularly when GA is required (e.g. head trauma patients). Advanced imaging and other diagnostic procedures may be possible in the non-anaesthetized animal if they are already stuporous or comatose.



▼ **113 Stepwise diagnostic approach to altered level of consciousness.**



▲ 114 (a) A comatose 1-year-old Domestic Shorthair cat presented following head trauma secondary to a dog attack 2 days previously. There was no response to a painful stimulus applied to the digit, and the cat had fixed and dilated pupils that were unresponsive to light. T1-weighted transverse (b), T2-weighted transverse (c), T2*-weighted transverse (d) and T2-weighted sagittal MR images (e) revealed a large poorly circumscribed lesion within the midbrain, consistent with haemorrhage and perilesional oedema associated with vermal herniation (arrows). The imaging characteristics of T1 isointensity, T2 hypointensity and marked T2* hypointensity would be consistent with deoxyhaemoglobin, typically seen around 1–3 days post haemorrhage. Diffuse damage to the RAS and CN III (oculomotor) nuclei are consistent with the loss of parasympathetic input to the eyes and the altered level of mentation. Fluid and soft tissue accumulation present within the left bulla was reflective of haemorrhage from the external ear at presentation (arrows in b and d).

The specific diagnostic tests for obtundation, stupor and coma are described below:

- **Magnetic resonance imaging.** MRI is the imaging modality of choice in most cases to help elucidate structural disease of the CNS parenchyma resulting in decreased mentation (**114**).
- **Computed tomography.** CT is particularly useful for investigation of head trauma where calvarial fractures are suspected. It is also the imaging modality of choice for determining the presence of acute haemorrhage (e.g. subdural haematoma), although most MRI scanners are able to detect this with gradient echo (T2*) sequences by the time imaging is undertaken.
- **CSF analysis.** This should be undertaken with great care in animals with suspected intracranial disease, but it may help to determine underlying causes of disease. Collection is preferably done following advanced imaging so that the presence of mass lesions and/or brain herniation can be assessed.
- **Brainstem auditory evoked response (BAER).** Assessment of the central auditory pathway allows indirect assessment of overall brainstem function. Complete loss of BAER is a poor prognostic indicator in comatose animals (assuming peripheral hair cells are functional). Middle latency auditory evoked responses (MLAERs) recorded from the cortex may be used to assess cortical function in addition to brainstem function.
- **Electroencephalography.** EEG allows for assessment of cortical function. Low amplitude or flat trace (0.5 mV) following auditory and painful stimuli carries a poor prognosis in comatose animals.
- **Somatosensory evoked potentials (SSEPs).** Recording of potentials from the head following stimulation of sensory nerves in a limb may be used to assess conduction of information to the cortex through the brainstem.

In a comatose animal:

- 'Flat' EEG plus loss of BAER/SSEP and MLAER is evidence of cerebral and brainstem death (**115**, see next page).
- 'Flat' EEG with loss of SSEP/MLAER and preservation of BAER suggests cerebral disease with preservation of brainstem function.
- Normal EEG with loss of BAER/SSEP and MLAER suggests brainstem disease with preservation of cerebral function.

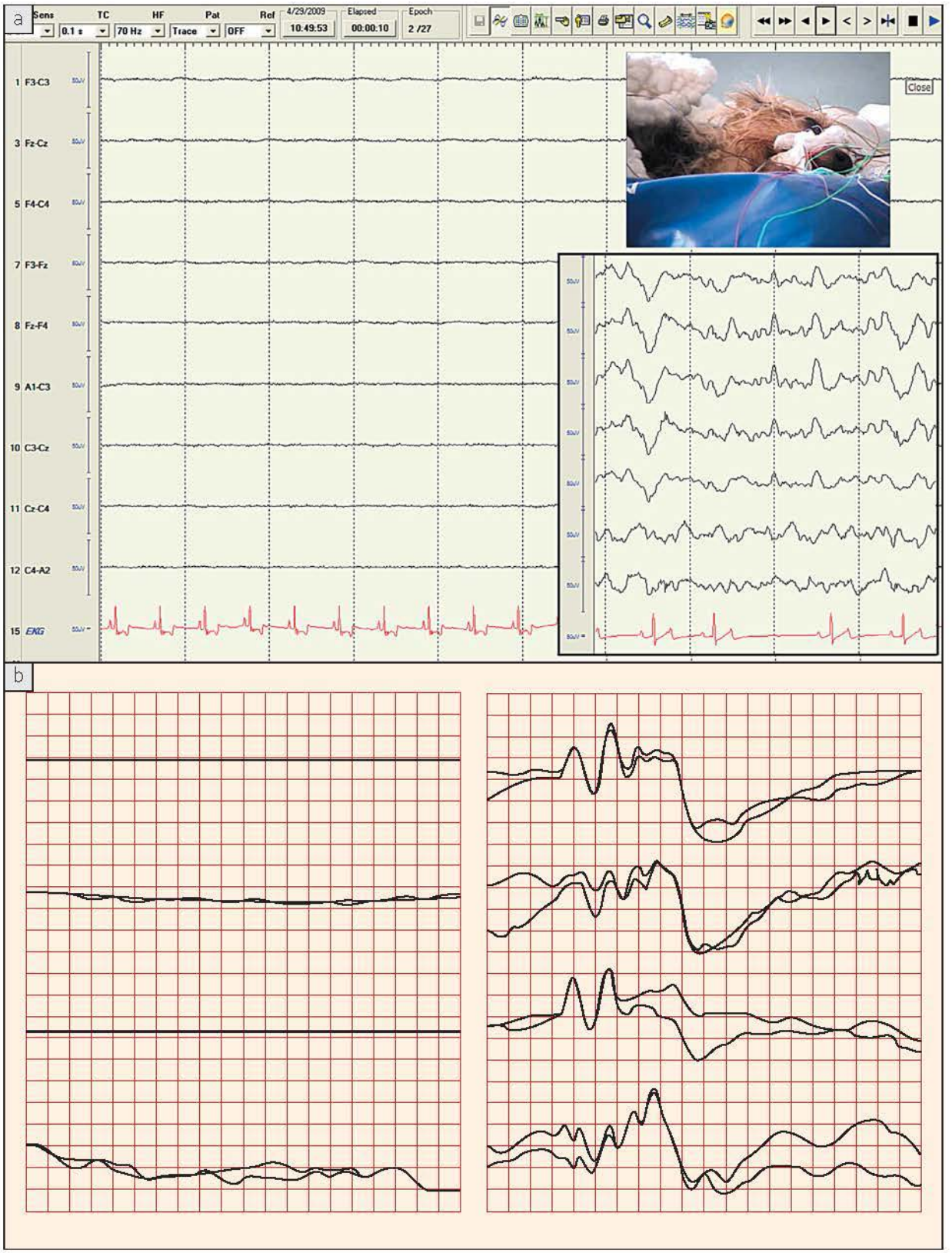
COMMON CAUSES OF OBTUNDATION, STUPOR AND COMA

Cerebrovascular accidents (Chapter 17), meningoencephalitis (Chapter 19), head trauma (Chapter 20), brain tumours (Chapter 26), metabolic encephalopathies (Chapter 27) and toxic encephalopathies (Chapter 28) are described in detail elsewhere in the book.

Hydrocephalus

Overview

Hydrocephalus is active distension of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the ventricles to its point of absorption in the systemic circulation. Loss of brain parenchyma may result in a secondary increase in ventricle size, which has been termed compensatory hydrocephalus or hydrocephalus ex vacuo. A congenital predisposition exists in many miniature breed dogs, Bulldogs and Boston Terriers. The condition may be congenital due to obstruction of ventricular drainage (often at the level of the mesencephalic aqueduct) or decreased absorption of CSF due to dysfunction of the arachnoid villi, or it may be the result of secondary obstruction due to acquired disease (e.g. neoplasia, infection or inflammation). Hydrocephalus may be secondary to CSF overproduction (e.g. choroid plexus tumour [rarely]) or increased viscosity of CSF due to elevated CSF protein content seen with some tumours and the 'dry-form' of FIP in cats.


a
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2 /27
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1 F3-C3
3 Fz-Cz
5 F4-C4
7 F3-Fz
8 Fz-F4
9 A1-C3
10 C3-Cz
11 Cz-C4
12 C4-A2
15 EKG
b

◀ **115** Electrophysiological findings from a comatose 10-year-old Yorkshire Terrier that failed to recover from anaesthesia. (a) Video EEG demonstrates essentially flat line tracings consistent with diffuse loss of cortical neuronal function. The ECG tracing can be seen at the bottom of the tracing. A normal EEG from a dog in slow wave sleep is inset for comparison. (b) BAER is also flat line consistent with loss of brainstem function (compare with normal animal, bottom right); however, damage to the peripheral hair cells could also result in similar recordings. The findings were consistent with a comatose animal with no brainstem reflexes.



▲ **116** A 5-month-old Chihuahua with congenital hydrocephalus. Clinical signs of decreased mentation, absent menace responses and postural reaction deficits in all limbs were consistent with diffuse loss of cortical tissue secondary to the hydrocephalus. A marked doming of the skull is apparent, as well as a typical ventrolateral deviation of the eyes. A persistent fontanelle was also palpable.

Clinical presentation

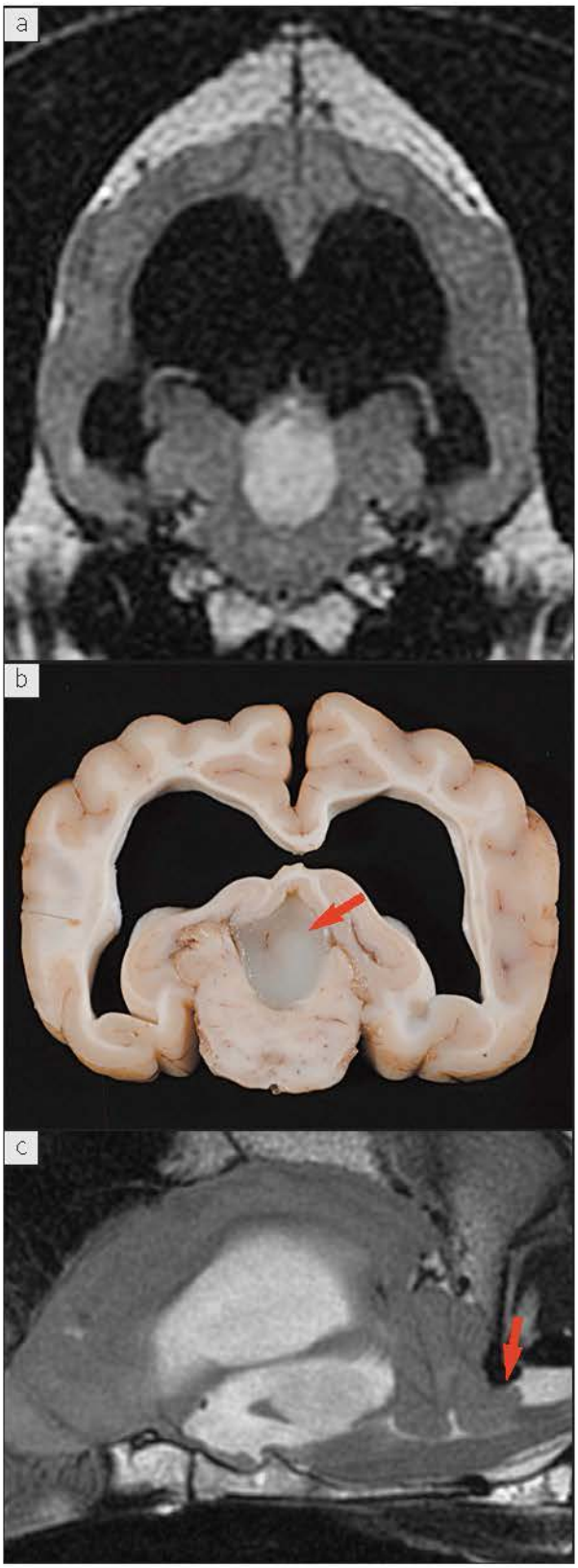
Hydrocephalus results in diffuse cerebral and/or brainstem signs due to cortical compression and elevated ICP. Most commonly, animals have altered mentation, inappropriate behaviour, cortical blindness and seizures. A ventrolateral strabismus is common. Hydrocephalus may be asymptomatic in milder cases. Congenitally affected animals often have skull deformity (dome-shaped) and persistent fontanelles (**116**).

Diagnosis

Pneumo/contrast venticulography has been superseded by alternative diagnostic techniques. Ultrasound can be used to define ventriculomegaly if a persistent fontanelle is present, and it has been used to assess the likelihood of developing clinical signs (**117**). CT and, particularly, MRI (**118**, next page) are the diagnostic modalities of choice. EEG may be suggestive of the diagnosis. Collection of CSF to aid in diagnosis of underlying diseases should be done with care due to the potential for brain herniation secondary to elevated ICP. Aspiration of CSF from an enlarged ventricle (via a fontanelle or hole made with a trochar), rather than from the cerebellomedullary cistern, may help to reduce this risk. Use of hyperosmolar agents immediately prior to collection may also be beneficial in this regard.

▼ **117** Ultrasound examination of the brain is possible when persistent fontanelles are present. Typically, enlarged lateral ventricles (V) are easily imaged with variable loss of overlying cerebral cortex. Brainstem structures such as the thalamus (Th) usually appear relatively unremarkable.





◀ 118 (a, b) Transverse fluid-attenuated inversion recovery MR image and corresponding gross necropsy image from a 2-year-old Golden Retriever with a low-grade astrocytoma invading the 3rd ventricle. Secondary hydrocephalus involving the lateral ventricles probably resulted in the animal presenting with signs of altered behaviour and decreased level of mentation. (c) Sagittal T2-weighted MR image obtained after the dog acutely decompensated and exhibited opisthotonus, rapid decline in mentation and respiratory arrest. Herniation of the cerebellum through the foramen magnum is present (arrow), resulting in compression of the underlying brainstem with compromise of the reticular activating system and the respiratory centres.

Management

Glucocorticoids may decrease CSF production, among other less well-defined effects, and provide long-term management in some cases (prednisolone, 0.25–0.5 mg/kg PO q12h). Other drugs that decrease CSF production, such as acetazolamide (0.1 mg/kg PO q8h) (carbonic anhydrase inhibitor) or furosemide (1–2 mg/kg PO q12h), are less well evaluated for the treatment of this condition. Osmotic agents (mannitol, hypertonic saline) may be used to decrease ICP as a short-term therapeutic measure. Seizure treatment may be necessary in many cases on a chronic and acute emergency basis.

Surgical treatment involves either resection of space-occupying mass lesions or placement of ventriculoperitoneal (VP) shunts. Optimal indications for management of VP shunts for dogs has not been well documented; infection, migration and obstruction of shunts are common complications, and no evidence of consistent long-term benefits over medical management has been published for dogs.

The prognosis is dependent on severity of neurological signs and rapidity of progression at presentation, as well as the ability to treat any underlying diseases. Specific and/or symptomatic treatment of mass lesions and oedema can result in marked clinical improvement in the short term. The prognosis for severe congenital hydrocephalus is usually guarded, as clinical signs (cortical atrophy) are often severe at presentation and medical/surgical management has limited benefit in many cases.

Hypoxia/global brain ischaemia

Overview

Ischaemia is a deficiency of blood flow to an organ or tissue resulting from diminished blood flow through a regional artery (i.e. infarct) or throughout the circulation. Hypoxia represents inadequate tissue oxygen supply for normal physiological function. It is often associated with ischaemia and hypoglycaemia, with resultant failure in energy supply. The brain (particularly neurons) has the highest energy requirement of any organ and minimal capacity for anaerobic metabolism. Global brain ischaemia usually affects a dense area of selectively vulnerable neurons in brain tissue. Lack of oxygen/cessation of blood flow results in unconsciousness within 5–10 seconds.

Neuronal cell death involves failure of energy metabolism and secondary effects of excitatory neurotransmitters, such as build-up of glutamate and aspartate, free radical formation and calcium influx. Specific anatomical areas, including the cerebral cortex, hippocampus, certain basal nuclei (e.g. caudate nuclei), thalamus and cerebellar Purkinje cell layers, are more susceptible to hypoxic injury.

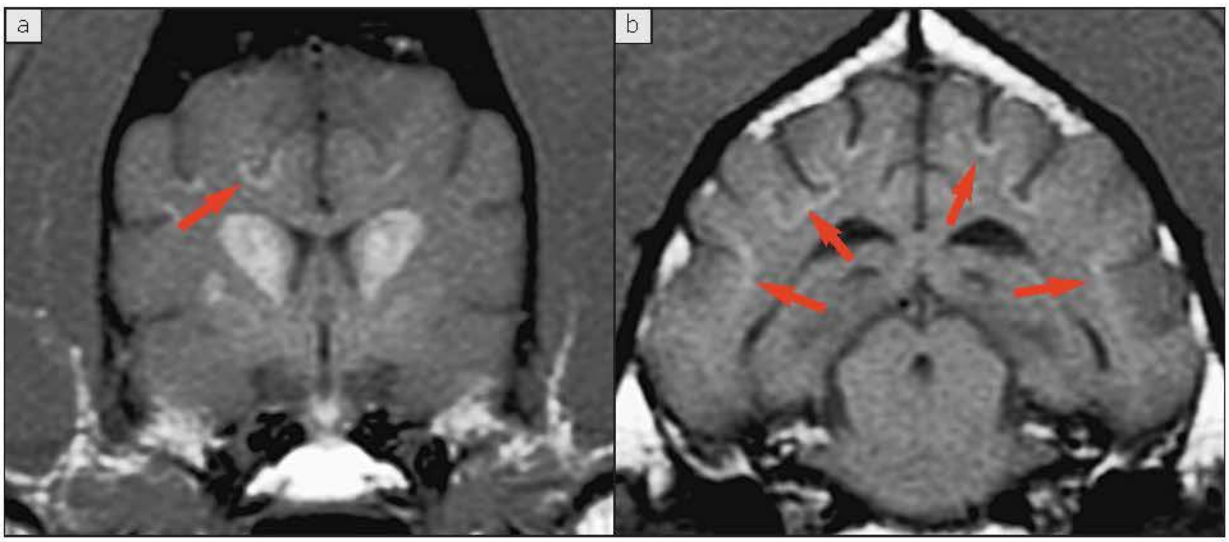
Common causes of hypoxia include anaesthetic-related accidents (cardiac arrest, inadequate oxygenation, hypotension), near drowning, prolonged seizure activity, smoke inhalation/carbon monoxide poisoning and ischaemia. Cardiovascular and respiratory disease may lead to transient hypoxia causing syncope.

Clinical presentation

Clinical signs may be localized following local ischaemia or infarction. Generalized hypoxia/ischaemia results in generalized pathology and symmetrical clinical signs. Decreased levels of consciousness are common, as are other signs referable to diffuse cortical disease such as seizures, blindness, menace loss, postural deficits and inappropriate behaviour.

Diagnosis

Diagnosis is often based on clinical signs and history. MRI may reveal symmetrical and often diffuse lesions involving 'vulnerable' structures such as the cerebral cortex, hippocampus and other grey-matter areas (**119**). Assessment of carbon monoxide toxicity requires a CO-oximeter.



▲ **119** Transverse T1-weighted MR images at the level of the caudate nuclei (a) and at the level of the midbrain (b). This 4-year-old Labrador Retriever presented for obtundation and inappropriate behaviour following an episode of prolonged status epilepticus and hyperthermia. Diffuse lesions involving the caudate nuclei bilaterally and specific laminae within the cerebral cortex (arrows) can be seen. Altered metabolism of highly vulnerable neurons in these grey-matter areas can result in diffuse cortical laminar and basal nuclei necrosis, with signs of diffuse cerebral disease.

Management

Treatment depends on addressing underlying diseases, seizure control if appropriate, oxygen supplementation/ventilation and general supportive care. The prognosis following global ischaemic damage is guarded, particularly if neurological deficits are severe, although some deficits may be reversible. Signs resulting from neuronal necrosis are almost always permanent. Recovery can take days to weeks and may be accompanied by severe behavioural abnormalities, which most probably reflect damage to cerebral cortical tissue.

Hypertension

Overview

Hypertension is represented by a consistently elevated BP (sustained systolic pressure >160 mmHg). It is most often secondary to underlying disease including renal disease, hyperadrenocorticism/glucocorticoid administration, diabetes mellitus, pheochromocytoma, hyperthyroidism, primary hyperaldosteronism and hepatic disease. Autoregulatory mechanisms (mostly arteriolar) regulate intracranial blood flow and protect local microcirculation up to approximately 180 mmHg. Beyond this level, microvascular hypertension/hyperperfusion results in interstitial oedema, with resultant elevations in ICP and hypertensive injury. Haemorrhagic infarcts may also occur. Cats are more sensitive than dogs to developing hypertensive encephalopathy, particularly with rapidly developing hypertension.

Clinical presentation

Clinical signs include seizures, ataxia, tremors, blindness, decreased mentation and abnormal behaviour (e.g. head pressing). Oedema may result in brain herniation (**120**), which is often fatal. Signs of other organ dysfunction secondary to the hypertension are likely, including retinopathy (retinal detachment and/or haemorrhage) (**120d**) and renal disease.

Diagnosis

Diagnosis depends on documentation of consistently elevated systemic BP with appropriate neurological signs +/- compatible advanced imaging evidence. MRI may reveal evidence of generalized oedema and/or ischaemic/infarctive disease. Identification of underlying diseases is essential for appropriate management.

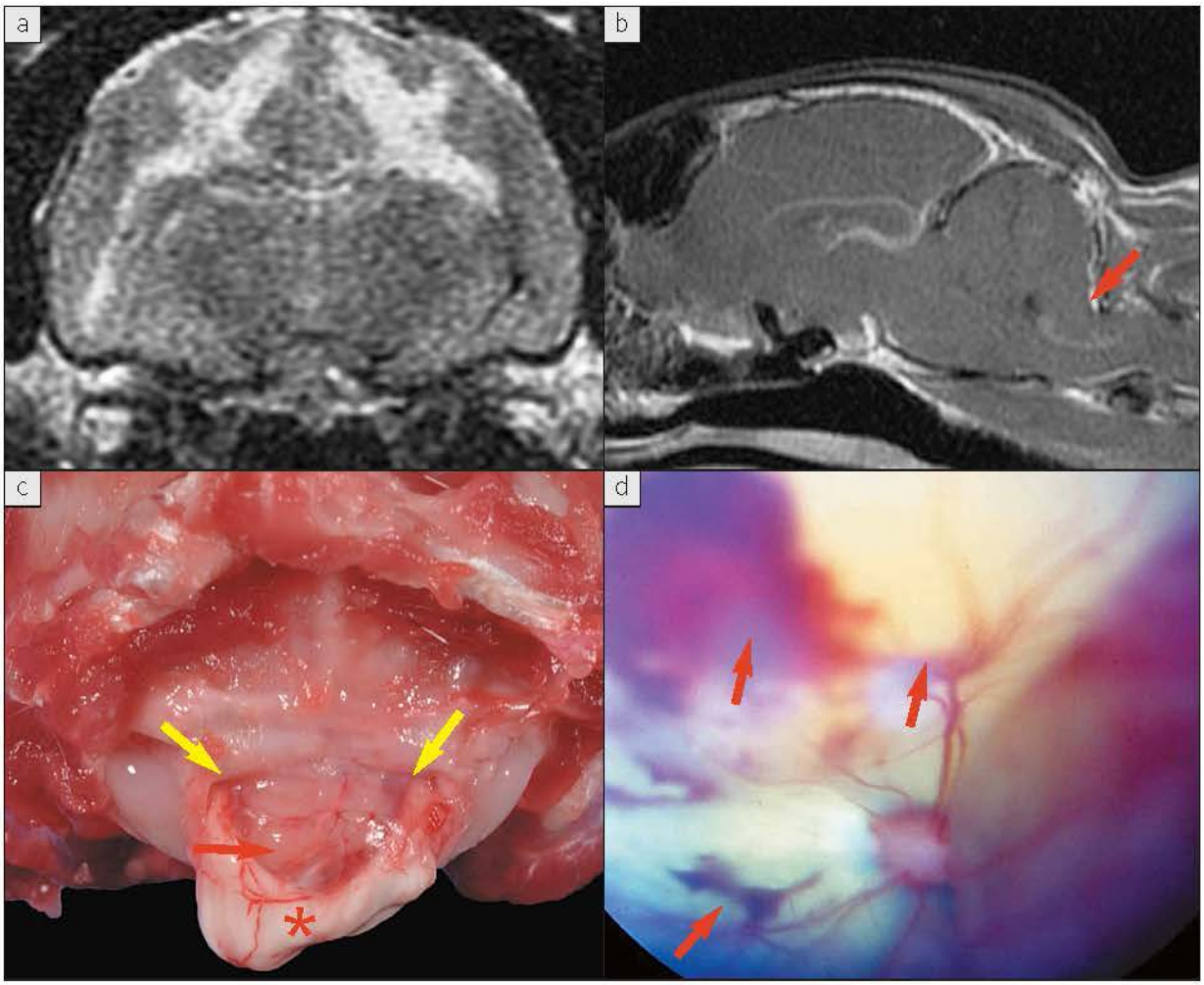
▶120 (a) Transverse FLAIR MR image at the level of the thalamus from a cat with hypertensive encephalopathy. Diffuse hyperintensity within the white-matter tracts is a typical MRI finding and is reflected in typical clinical signs such as decreased level of mentation. (b) Sagittal T1-weighted post-contrast MR image showing herniation of the cerebellum. Herniation with subsequent brainstem compression was suspected to have resulted in an observed acute decrease in mentation from obtundation to stupor. The presenting obtundation was presumed to have been caused by the diffuse cerebral disease seen on the FLAIR image. (c) Gross pathology showing herniation of the cerebellar vermis (red arrow) through the foramen magnum (yellow arrows), with compression of the brainstem (asterisk). (d) Sustained systolic blood pressure over 200 mmHg resulted in multiple organ pathology, including retinal separation. There are multiple areas of haemorrhage (arrows) throughout the fundic layers and separation of the retina (predominantly dorsally). (c, d courtesy UC Davis Ophthalmology Service)

Management

Treatment is usually aimed at addressing the underlying cause (if identified) and symptomatic treatment of systemic hypertension, which may be continued indefinitely. Amlodipine (a calcium channel blocker) (0.1–0.25 mg/kg PO q12–24h) is the most commonly recommended antihypertensive drug for cats, and amlodipine or an angiotensin-converting enzyme inhibitor such as enalapril (0.25–0.5 mg/kg PO q12h) (alone or in combination) is recommended for dogs. Beta and alpha adrenergic blockers are used less commonly.

In severely neurological animals with rapid decompensation, hyperosmolar agents, such as mannitol, may be beneficial in reducing cerebral oedema and ICP. Ideally, these agents should not be used until BP has been normalized, as they can cause transient increases in BP. Correction of hypertension can result in rapid improvement of neurological function.

The long-term prognosis is often dependent on the ability to manage both the hypertension and the underlying disease process.



Narcolepsy/cataplexy

Overview

Narcolepsy/cataplexy is a chronic sleep disorder characterized by excessive daytime sleepiness and cataplexy (sudden loss of muscle tone in response to emotional stimuli). Both familial and sporadic narcolepsy occur in dogs and both are associated with defective hypocretin/orexin neurotransmission. It is rarely reported in cats.

Clinical presentation

Clinical signs include excessive sleepiness, with disrupted sleep/wake patterns (difficult to document in most dogs since frequent sleeping is common normally), and, more clinically important, pronounced attacks of cataplexy. Cataplectic episodes are usually triggered by emotional stimuli, particularly food, and may last from seconds to minutes. Collapses may be complete or result in staggering. Animals may remain conscious or fall into rapid eye movement (REM) sleep (particularly with prolonged attacks). Muscles are always flaccid, in contrast to seizure disorders where increased muscle tone is often present. Autonomic signs such as urination, salivation and defecation are not seen.

Diagnosis

Diagnosis is based on clinical signs; EEG is useful to show that attacks are associated with recordings typical of wakefulness or REM sleep rather than slow-wave sleep. EEG is also important in ruling out the presence of paroxysmal activity such as abnormal spikes and waves consistent with a seizure disorder.

Animals with familial narcolepsy (typically Dobermanns, Labradors, Dachshunds) have defects in the hypocretin-1 receptor 2 gene with normal CSF hypocretin-1 levels. Dogs with acquired narcolepsy have decreased CSF hypocretin-1 levels (less than 80 pg/ml; reference 250–350 pg/ml).

Management

Narcolepsy is not life threatening; however, the cataplectic attacks can be debilitating and frustrating for owners. Common sense precautions, such as provision of elevated water and food bowls, should be taken. Simple modification of daily routines, such as not allowing competition during feeding, can reduce frequency of attacks.

CNS stimulants, such as D-amphetamine and modafinil, may decrease daytime sleepiness; however, management of cataplectic attacks using drugs that inhibit adrenergic reuptake, such as the tricyclic antidepressants clomipramine (3.0–6.0 mg/kg PO q24h), imipramine (0.5–1.0 mg/kg PO q8–12h), desipramine (3 mg/kg PO q12h) and the alpha-2 antagonist yohimbine (0.05–0.3 mg/kg PO q12h), is clinically more important.

A recent report has described the successful use of venlafaxine (2.5 mg/kg PO q24h), which is an arylalkanolamine serotonin-norepinephrine reuptake inhibitor.

Intrathecal delivery of hypocretin-1 has not been shown to be effective in sporadically occurring narcolepsy in dogs.

SEIZURES

Simon Platt

INTRODUCTION

Epileptic seizures are sudden onset (paroxysmal) clinical events that represent an abnormality of forebrain neurotransmission. Epilepsy is characterized by recurrent epileptic seizures and therefore implies a less transient aetiology. The underlying abnormality can be due to structural or chemical interference with the normal 'balance' that exists in the brain between neuronal excitation and inhibition. Disruption of this balance may result in other clinical signs referable to forebrain dysfunction, such as behavioural and visual abnormalities, but this is not necessarily the case and the affected dog or cat could be completely neurologically normal apart from the seizure activity.

Unfortunately, a disturbance of the electrical circuitry in the nervous system, whether structural or functional (neurochemical), may result in other paroxysms that can closely resemble seizure activity. These include narcolepsy, cataplexy, movement disorders (dyskinesias), sleep disorders and tremor syndromes. Tremors and involuntary movements are further discussed in Chapter 13. Further to disorders of the CNS, disorders of peripheral nerves and muscles, the respiratory and cardiovascular systems and systemic metabolism may result in paroxysmal 'collapses', which must also be considered when the possibility of a seizure event has been raised.

It is extremely important to distinguish the nature of the paroxysm, as this will determine the most appropriate diagnostic and therapeutic actions and, in the case of seizure activity, immediately confirm a forebrain localization. It is therefore necessary to ask the question: what is a seizure? The answer lies in the description of the event, which is often only seen by the owner, as well as the circumstances that surround its onset (*Table 35*, next page). It is therefore important to know the typical clinical characteristics (phenotypes) of seizures, so that the owner can be asked the most appropriate questions about the event.

The phenotypic nature of epileptic seizures

The stages of seizure activity

There are four recognizable stages of seizure activity, which can be vital when trying to differentiate a seizure event from other episodic activity such as syncope or neuromuscular weakness. The more seizure events that the dog or cat exhibits, the more likely it is that the owner will be able to recognize these stages. The stages consist of the prodrome, aura, ictus and post-ictal period:

- **The prodrome** is a behavioural phenomenon that precedes the onset of a seizure by hours to days and is manifested by hiding, restless activity or fearful behaviour.
- **An aura** is a subjective sensation that marks the onset of a seizure. This is obviously difficult to recognize in dogs and cats unless it is presumed that vomiting, salivation or inappropriate urination seen prior to an obvious seizure event is classed as the aura. Subtle changes in behaviour before a seizure may be indicative that the animal is experiencing an aura.
- **The ictus** is the seizure event itself (see below).
- **The post-ictal period** is characterized by atypical behaviour that immediately follows the seizure. The behaviour seen may include restlessness, aggression, delirium, lethargy, confusion, visual loss, thirst, hunger and inappropriate urination. This may last for hours in some animals regardless of the underlying cause of the seizure. It is essential to discuss this period with the owner, as it is not seen with narcolepsy/cataplexy, neuromuscular collapse or movement disorders. Short periods of confusion and visual dysfunction may be apparent after a syncopal event, depending on the severity of the underlying cardiovascular cause.

Table 35 **Differentiation of non-epileptic paroxysmal events from epileptic seizures**

PAROXYSMAL EVENT	PRECIPITATING FACTORS	LEVEL OF CONSCIOUSNESS	FLACCID OR SPASTIC COLLAPSE
Narcolepsy	Excitement/feeding	Absent	Usually accompanied by cataplexy
Cataplexy	Excitement/feeding	Normal, if not accompanied by narcolepsy	Flaccid
Neuromuscular collapse	Activity/exercise	Normal unless impaired by respiratory compromise	Often flaccid (e.g. myasthenia gravis). Can appear spastic in some cases of myopathy
Syncope	Exercise, excitement, cough	Reduced to absent	Flaccid
Movement disorder	None, to excitement/activity/exercise	Normal	Often spastic
Metabolic collapse (e.g. hypoglycaemia)	May be related to feeding times/excitement	Variable; long lasting	Often flaccid. Can be spastic in some cases (e.g. hypocalcaemia)
Sleep disorder	Sleep	Absent (REM sleep) and may progress to apparent wakefulness during event	Either
Vestibular event	Variable	Normal to depressed	Usually spastic

The ictal event

The description of the ictus can go a long way to confirming that the animal is indeed exhibiting seizure activity as opposed to syncope or neuromuscular collapse. The ictal event usually lasts for 60–90 seconds. Should this event last for longer than 5 minutes, then it is termed status epilepticus (see Chapter 23). However, it is not unusual for the owner to be unable to determine the length of the event itself and to frequently overestimate this experience. The event should be peracute in its onset and stereotypical (i.e. its characteristics are identical each time it occurs). This is obviously different from neuromuscular collapse. Most ictal events also have no identifiable precipitating event, occurring most commonly from sleep or at rest. This distinguishes seizure activity from narcolepsy/cataplexy, which is precipitated by excitement, and from syncope and neuromuscular collapse, which are precipitated by activity.

The ictus can be classified into two major phenotypic categories: generalized and focal.

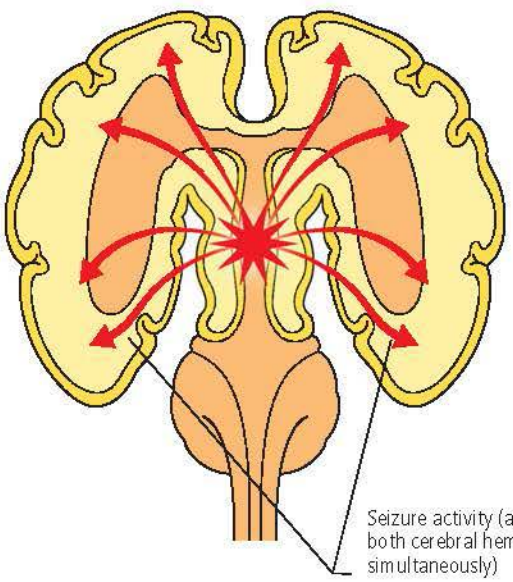
Generalized seizures

Generalized seizures indicate involvement of both cerebral hemispheres simultaneously (**121**). Consciousness is often impaired and motor manifestations are bilateral. Generalized seizures may have one or several of the following phases, with a combination of tonic–clonic activity being the most common:

- **Tonic:** sustained, increased muscle contraction; the animal usually becomes recumbent in this phase (**122**).
- **Myoclonic:** sudden, brief, involuntary, single or multiple contractions of muscles or muscle groups.
- **Clonic:** regularly repetitive myoclonus, which involves the same muscle groups, and is prolonged.
- **Atonic**: sudden loss of muscle tone, usually lasting 1–2 seconds or more.

INVOLUNTARY MOVEMENT DURING EVENT	POSSIBLE HISTORICAL FINDINGS	POSSIBLE PHYSICAL EXAMINATION FINDINGS
No	Often purebred dog with early age onset	Normal
No	As for narcolepsy	Normal
May appear to be present when attempting to stand	May be accompanied by dysphagia, dysphonia, regurgitation	May be normal or may be muscle atrophy, muscle pain and/or reduced reflexes
No	May be accompanied by cough, increased respiratory noise	Arrhythmia, pulse deficits, murmur, abnormal lung auscultation, cyanosis
Yes; exacerbated by attempts to stand	May be purebred with early age onset	Normal
No, except facial twitching in some cases of hypoglycaemia or hypocalcaemia	Anorexia, depression, polyuria, polydipsia, vomiting, weight loss	May be normal; weight loss
Yes; REMs during event	Never occurs during periods of normal consciousness	Normal
Attempts to stand; nystagmus	Periods of head tilt and/or ataxia; head tremor; ear disease	Normal to nystagmus, head tilt, ataxia, vomiting

▼ **121** **Generalized seizure activity results from a synchronized electrical discharge from the whole of the forebrain.**





▲ **122** **Generalized seizures most commonly present with the animal in lateral recumbency exhibiting tonic–clonic movements. The limbs are most consistently in rigid extension (tonic), as seen in this Bull Terrier, with the intermittent involuntary muscle contractions superimposed appearing to cause a flexor 'paddling' motion.**

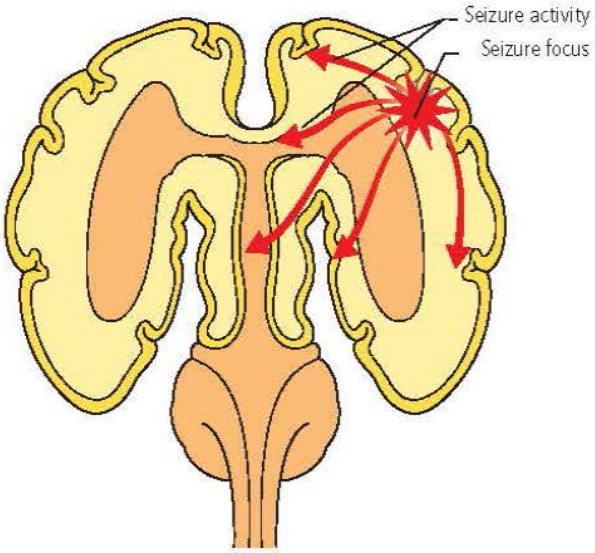
Focal seizures

A focal seizure is due to initial activation of only one part of one cerebral hemisphere or specific region in the forebrain, such as the hippocampus (**123**). Compared with dogs, cats more commonly exhibit focal seizures. Any portion of the body can be involved during a focal seizure, depending on the region of the brain affected (**124**). The focal clinical signs may be associated with a higher incidence of focal intracranial pathological change in cats, but are apparently quite often associated with idiopathic epilepsy in dogs. If there is an alteration in the animal's awareness during the event, it is called a complex focal seizure (previously termed psychomotor seizures).

The various forms of focal seizure depend on where in the forebrain the neurotransmission abnormality occurs. These forms include:

- **Focal motor seizures.** These are (1) elementary motor events, which consist of a single type of stereotyped contraction of a muscle or group of muscles or (2) automatisms. Automatisms are movements that resemble voluntary motor movements and include chewing activity and rhythmic contractions of a single limb. Consciousness is often unaffected during focal motor seizure activity, but it is difficult to assess whether this is the case in many patients.
- **Focal sensory seizures.** These are behavioural seizures involving the limbic system. They may present as rage, aggression without provocation, fly-catching, running in circles, floor licking, vocalization and tail chasing. An aura that does not evolve into loss of consciousness is a focal sensory seizure.
- **Focal autonomic seizures.** These seizures are apparently rare and cause predominantly autonomic signs such as vomiting, diarrhoea and abdominal pain. A syndrome characterized by drooling, dysphagia and painful enlargement of the mandibular salivary glands is probably a form of focal autonomic seizure.

A seizure may start focally and ultimately spread throughout both cerebral hemispheres, resulting in secondary generalization, which the owner may not notice until the animal has exhibited several such events.

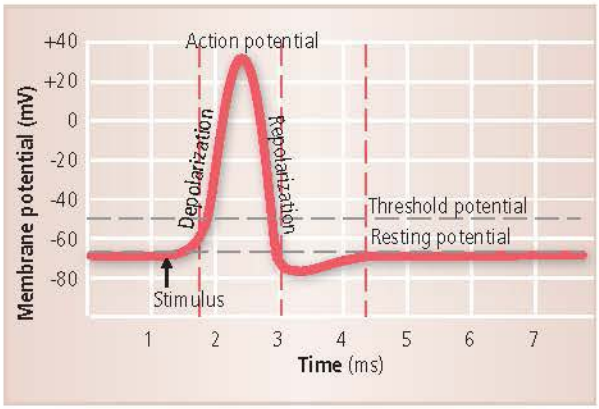


▲ **123** **Focal seizure activity results from an abnormal electrical discharge in a single area of the brain. The area from which the focus originates determines the clinical characteristics of the focal seizure.**

▼ **124** **Focal motor seizure activity can be manifested by rhythmic contractures of the muscle of a single limb, as seen in the right hindlimb of this cat, which exhibited this form of seizure activity frequently throughout the day.**



▶ **125** An action potential is generated by a flow of positively charged sodium ions across the neuronal membrane, triggered by environmental stimuli or the release of neurotransmitters. This causes the membrane to depolarize, bringing the membrane from the resting potential (about -70 mV) up to the threshold potential (about -55 mV). As the action potential is triggered, the membrane potential abruptly rises and then falls, often below the resting level, as a compensatory flow of potassium ions leaves the cell. Action potentials can occur 10–100 times per second.



Neuroanatomical basis of seizure activity

An epileptic seizure definitively implies a disorder of the forebrain. Therefore, it is extremely important to be sure that a seizure is suspected, as the underlying causes and subsequent investigations are vastly different from those considered for cardiovascular and neuromuscular 'events'. Their causes may originate outside (extracranial) or inside (intracranial) the brain. Intracranial causes may be further subdivided into functional disorders (where no gross structural changes are evident in the brain and the cause is probably a neurochemical dysfunction) and structural disorders (where there is a gross structural cause within the brain [e.g. a brain tumour or hydrocephalus]). Extracranial causes include toxicities and metabolic disturbances that either interfere with CNS function or are directly neurotoxic.

Pathophysiology of seizure activity

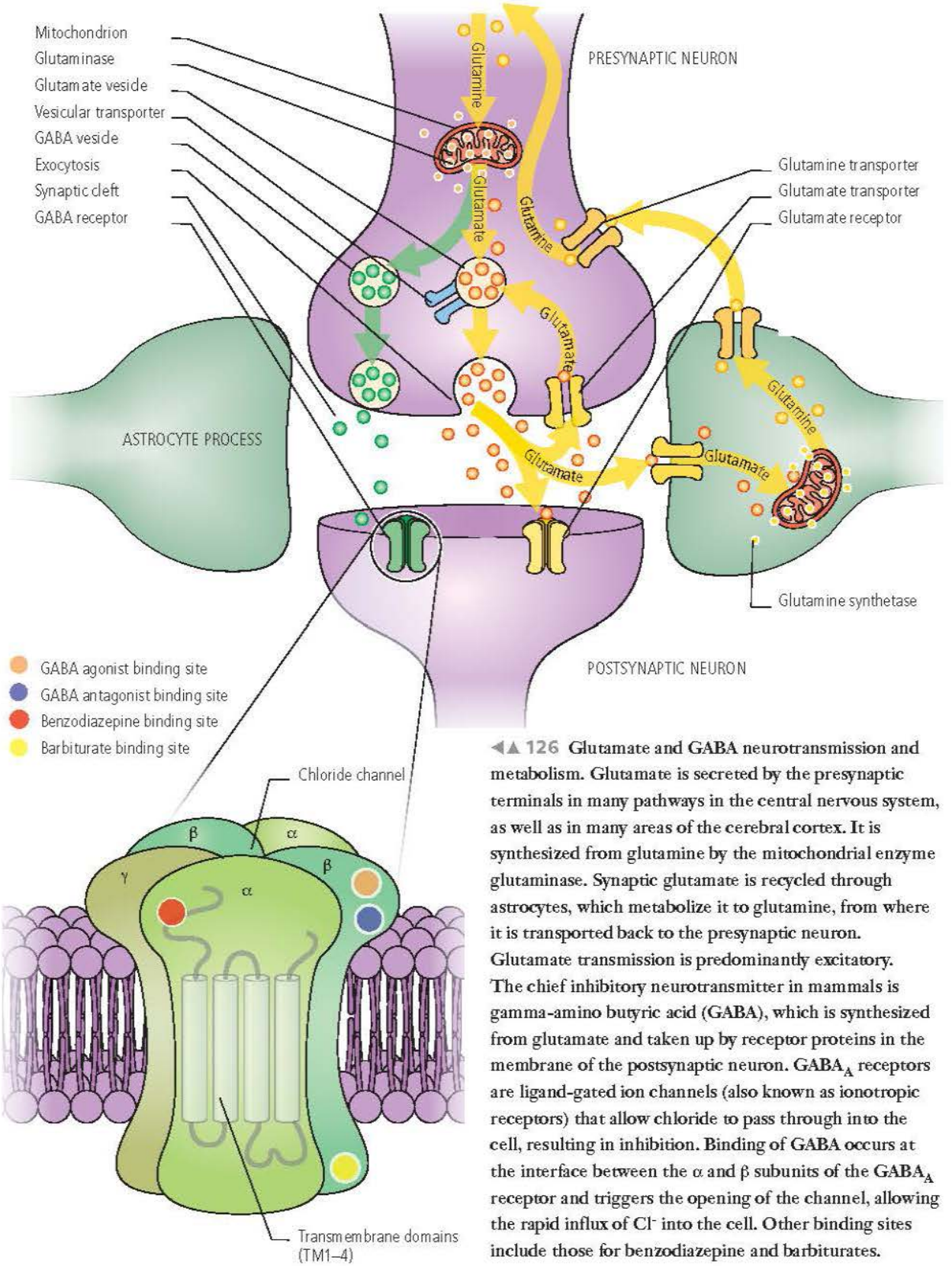
Irrespective of the fact that epilepsy can be caused by a variety of intracranial structural, cellular or molecular conditions and manifest itself in different ways, the epileptic seizure always reflects abnormal hypersynchronous electrical activity of neurons in the forebrain.

How electrical and neurochemical events within neurons culminate in a seizure, and what events are responsible for the termination of a seizure, are questions with no definitive answers. It is, however, clear that seizures are linked, at the lowest level, to membrane potentials, ionic fluxes and action potential generation. It has been suggested that seizure activity is ultimately due to an imbalance between excitation and inhibition, with increased excitation or decreased inhibition leading to epileptiform activity in the brain.

In neurons, action potential generation (**125**) results primarily from changes in the membrane permeability to four ions: sodium (Na^+), chloride (Cl^-), calcium (Ca^{++}) and potassium (K^+). These ions enter and exit neurons by way of voltage-dependent channels. The maintenance of membrane potential and transient changes in ion flux that culminate in the generation of an action potential are entirely dependent on the tight regulation of the above mentioned ions into neurons. Thus, changes or abnormalities in the regulation or activity of these ions could have a dramatic impact on the excitability and 'epileptogenicity' of individual neurons. Because virtually all neurons have the ability to fire in a rapid, repetitive fashion, it is clear that generating a recurrent cycle of membrane depolarizations and action potentials may be critical to the initiation and propagation of a seizure discharge.

Seizure propagation may be especially likely in neurons with intrinsic firing (bursting) abilities (such as those in the cortex and hippocampus) if the balance between excitatory or inhibitory inputs is altered. In the absence of appropriate inhibitory regulation, these populations of neurons may begin to fire synchronously, leading to a seizure. It is hypothesized that a population of neurons within an epileptic focus in the cortex undergoes paroxysmal synchronous depolarization, termed a paroxysmal depolarizing shift (PDS), which results in an abnormal burst of action potentials that continue in synchronous volleys without appropriate inhibition.

As neuronal action potentials result from the action of neurotransmitters, such as glutamate and gamma-aminobutyric acid (GABA), released by presynaptic terminals, abnormalities of these neurotransmitters and



◀▲ **126 Glutamate and GABA neurotransmission and metabolism.** Glutamate is secreted by the presynaptic terminals in many pathways in the central nervous system, as well as in many areas of the cerebral cortex. It is synthesized from glutamine by the mitochondrial enzyme glutaminase. Synaptic glutamate is recycled through astrocytes, which metabolize it to glutamine, from where it is transported back to the presynaptic neuron. Glutamate transmission is predominantly excitatory. The chief inhibitory neurotransmitter in mammals is gamma-amino butyric acid (GABA), which is synthesized from glutamate and taken up by receptor proteins in the membrane of the postsynaptic neuron. $GABA_A$ receptors are ligand-gated ion channels (also known as ionotropic receptors) that allow chloride to pass through into the cell, resulting in inhibition. Binding of GABA occurs at the interface between the α and β subunits of the $GABA_A$ receptor and triggers the opening of the channel, allowing the rapid influx of Cl^- into the cell. Other binding sites include those for benzodiazepine and barbiturates.

their receptors have been implicated in the generation of seizures. Glutamate is the main excitatory neurotransmitter and GABA is the main inhibitory neurotransmitter in the brain (**126**). Normally, the excitatory post-synaptic potentials in neurons are followed immediately by inhibitory transmission due to GABA. If excitatory mechanisms dominate, initiated by either increased excitation or decreased inhibition, neurons become hypersynchronized, capturing more and more neurons and generating an epileptic seizure (**127**). Perpetuation of the seizure activity is possibly due to a vicious cycle whereby glutamate initiates widespread neuronal excitement, which can lead to neuronal damage and death, which contributes to further glutamate release. It is widely believed that the neurotoxic effects of glutamate stem in part from alterations in Ca^{++} permeability, which result in an increase in intracellular Ca^{++} levels. Dramatic elevations in Ca^{++} concentrations may induce a cascade of Ca^{++}-dependent intracellular events, such as activation of proteases and lipases, influx of other cations, such as sodium, and osmotic swelling of neurons that culminates in cell death. These cellular pathways are almost certainly responsible for the seizure-induced excitotoxicity present in prolonged seizures and ultimately enlarge the seizure focus, potentiating more frequent and severe seizures, such as status epilpeticus and clustering.

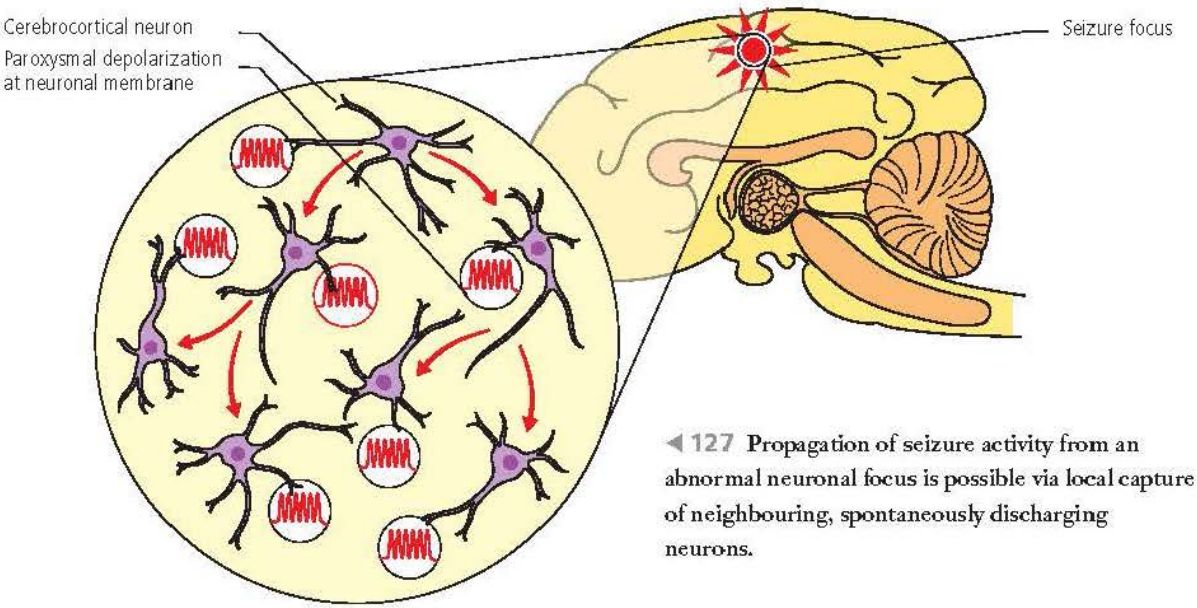
Studies in idiopathic epileptic dogs have confirmed there to be significantly less GABA and more glutamate in the CSF compared with normal controls. However, CSF neurotransmitter concentrations do not necessarily correlate with the synaptic concentration in the brain.

The mechanisms responsible for the 'arrest' of seizure activity are poorly described, but supposedly relate to the accumulation of lactic acid during the seizure. A breakdown in the mechanisms of seizure arrest, in addition to the evolution of seizure-induced excitotoxicity, forms the basis of the pathophysiology of status epilepticus.

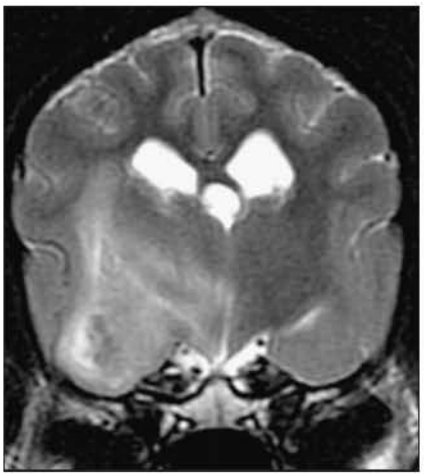
NEUROLOGICAL EVALUATION OF THE SEIZURE PATIENT

Seizures are aetiologically categorized as idiopathic, symptomatic or reactive. Regardless of their cause, they all ultimately represent dysfunction of the forebrain. Recognizing this aetiological classification scheme can help with interpretation of the neurological examination of the seizure patient.

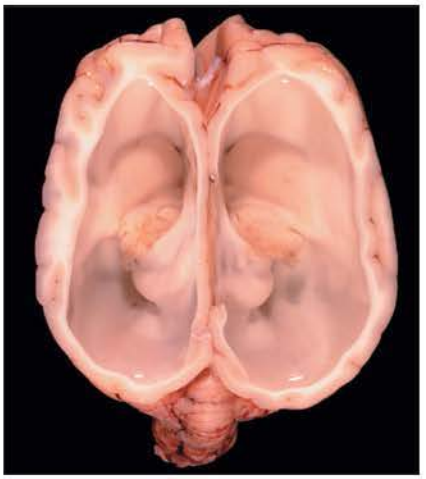
- **Idiopathic seizures.** The term idiopathic implies a suspected genetic basis for the seizure activity for which the underlying disorder is frequently suspected to be a transient functional or neurochemical abnormality. There are no identifiable structural abnormalities of the forebrain.



◀ **127 Propagation of seizure activity from an abnormal neuronal focus is possible via local capture of neighbouring, spontaneously discharging neurons.**



▲ 128 A transverse T2-weighted MR image of a 7-year-old dog with a hyperintense heterogeneous lesion in the piriform lobe, which was confirmed to be an astrocytoma.



▲ 129 A dorsal sectioned gross view of the brain from a 3-month-old Chihuahua that was euthanized following frequent seizures. Note the marked bilateral ventricular dilation compatible with hydrocephalus. (Photo courtesy Raquel Rech)

▶ 130 Marked lateral body curvature and a head turn in a young dog with a lateralized forebrain lesion.

- **Symptomatic seizures.** This term is often used to describe seizures resulting from a structural intracranial cause (e.g. brain tumours [**128**], inflammation or hydrocephalus [**129**]), which causes structural damage to the forebrain. A seizure focus that is not compatible with an idiopathic origin, but is not readily identifiable as a structural defect on MRI and CSF analysis, is referred to as cryptogenic.
- **Reactive seizures.** This term is often used to describe seizures resulting from an extracranial cause and includes metabolic and toxic disorders. As mentioned above, these ultimately cause seizure activity due to secondary interference with cerebral metabolism or, more directly, as primary neurotoxic insults. There are no identifiable structural abnormalities of the brain, but the functional impairment is global and exists as long as the aetiology exists.

Normal and abnormal forebrain function

The forebrain is important for normal behaviour, interpreting conscious sensory stimuli, vision and maintaining normal alertness. In addition to seizure activity, lesions of the forebrain may result in:

- Altered behaviour.
- Contralateral conscious sensory deficits. These include decreased contralateral facial sensory awareness (facial hypalgesia), contralateral conscious proprioceptive deficits and the so-called 'hemi-neglect'.
- Central blindness (blind with intact PLRs).
- Decreased levels of consciousness, typically to the level of a stupor, coma in animals usually being associated with brainstem lesions.



- Circling. In the majority of cases this is ipsilateral, but can be contralateral with certain cerebral lesions.
- Head turn (i.e. not a head tilt, as the ears are still horizontal). This usually occurs ipsilateral to the lesion (**130**).

Aims of the neurological examination in the seizure patient

A thorough neurological examination is essential to detect abnormalities other than the seizures; it will help with an aetiological classification and development of a differential diagnosis list. The examination may reveal (1) no abnormalities; (2) diffuse/symmetrical forebrain abnormalities; (3) focal/asymmetrical forebrain abnormalities; or (4) multifocal CNS abnormalities.

A completely normal neurological examination is compatible with idiopathic epilepsy. Symptomatic epileptic patients may also have a normal neurological examination if the causative lesion is located in the 'clinically silent' areas of the forebrain, such as the olfactory bulbs. During the early stages of a slowly enlarging mass in such a region, seizures may be the only clinical signs, but in time other neurological deficits related to the site will develop. Occasionally, metabolic disease may wax and wane, resulting in a normal neurological examination. However, many such patients will have concurrent systemic signs such as weight loss, polyuria or anorexia.

Diffuse, symmetrical forebrain abnormalities should prompt consideration of an extracranial cause (reactive epileptic seizures) (e.g. a metabolic encephalopathy such as hypoglycaemia or hepatic encephalopathy). If the patient is examined shortly after a seizure, such abnormal clinical signs may represent transient functional disturbances related to the seizure itself (see below).

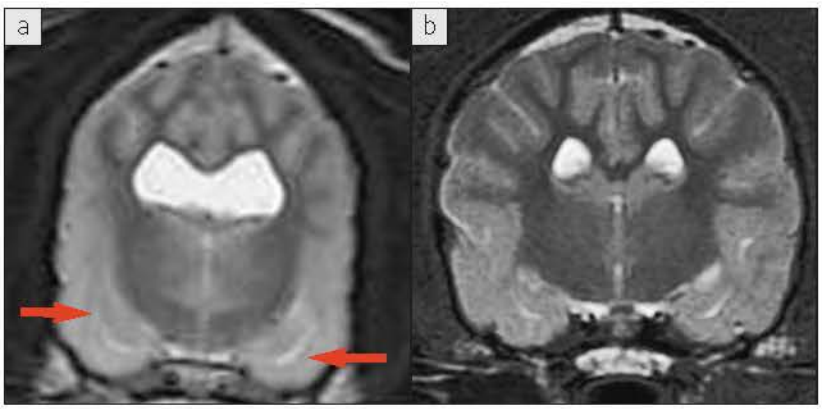
Focal/asymmetrical forebrain abnormalities are suggestive of a structural intracranial cause of the seizures (symptomatic epilepsy).

Multifocal CNS abnormalities are also suggestive of symptomatic epilepsy, but essentially narrow the differentials down to inflammation and metastatic neoplasia.

Neurological deficits arising as a consequence of seizures (post-ictal signs)

One of the features of idiopathic epilepsy is the absence of neurological deficits in the inter-ictal period. Therefore, where abnormalities are present in the inter-ictal period this would usually exclude idiopathic epilepsy from the differential diagnosis list. However, there are two exceptions to this:

- Depression of forebrain activity occurs during the period immediately following an epileptic seizure (so-called post-ictal depression). During this period, subtle neurological deficits, including conscious proprioceptive deficits, may be evident. Post-ictal depression lasts a variable amount of time, but most cases return to normal a few hours (up to a day) following the seizure episode.
- Neurological deficits may also result secondary to severe or prolonged seizures due to hypoxic injury or the so-called excitotoxicity phenomenon. Such lesions are particularly evident in the *N*-methyl-D-asparate (NMDA)-rich regions of the brain, such as the hippocampus, in the piriform lobes and, in severe cases, in the grey matter adjacent to the hippocampus (**131**).



◀ **131** (a) Transverse T2-weighted MR image of a dog 24 hours after a protracted generalized seizure. The piriform lobes bilaterally exhibit hyperintensity (arrows) suggestive of oedema secondary to the seizure activity. (b) Normal transverse T2-weighted MR image for comparison.

DIFFERENTIAL DIAGNOSES FOR EPILEPTIC SEIZURES

Prior to consideration of the differentials of forebrain disease as the cause of seizure activity, the clinician should be as comfortable as possible that the event described by the owner, or witnessed first-hand, is actually a seizure rather than one of the several clinical 'mimics' of seizure activity (*Table 35*). This will dramatically affect the subsequent diagnostic investigation and further therapeutic interventions. This determination is based on the phenotypic characterization of the event and historical confirmation of the potential precipitating events. Detailed questioning of the owner will be necessary.

Although generalized tonic–clonic seizures have a fairly unequivocal description, recognition of a focal seizure can pose a real challenge to the clinician. For this reason, video footage obtained by the owner of the paroxysmal event can be of tremendous help.

An epileptic seizure can be suspected based on:

- The peracute and unexpected onset and offset.
- Stereotypical pattern of each event.
- Presence of involuntary motor activity and/or abnormal mentation and behaviour and/or autonomic signs (salivation, urination and/or defecation). There is also notably increased muscle tone accompanying limb movement or collapse in most cases, which helps to differentiate seizures from other forms of collapse such as syncope.

Absolute confirmation of the epileptic nature can only be obtained by observing simultaneously the characteristic EEG changes and physical manifestation of the seizures.

The differential diagnosis for epileptic seizures is based on the signalment and history and the neurological examination suggesting idiopathic, symptomatic or reactive disease. The age of the patient may indicate the likely combination of differentials (*Tables 36*, *37* and *38*).

Table 36 **Differential diagnosis of seizure activity in patients <6 months old**

DISEASE MECHANISM	DOGS	CATS
Vascular	Rare	Rare
Inflammatory/infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial, rabies)* Meningoencephalitis of unknown aetiology (GME, necrotizing, idiopathic)*; rare at this age	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, *Cryptococcus*)* Meningoencephalitis of unknown aetiology (presumed immune mediated); rare
Trauma*	Frequent	Frequent
Toxic*	Frequent	Frequent
Anomalous	Hydrocephalus*	Infrequent
Metabolic	Hepatic encephalopathy* Hypoglycaemia* Hypocalcaemia	Hepatic encephalopathy
Idiopathic	Very rare at this age	Very rare at this age
Neoplastic	Very rare at this age	Very rare at this age
Nutritional	Thiamine deficiency	Thiamine deficiency
Degenerative	Lysosomal storage disease Intrinsic metabolic disorders (e.g. L-2-hydroxyglutaric aciduria)	Lysosomal storage disease

* Common cause

Table 37 **Differential diagnosis of seizure activity in patients 6 months to 6 years old**

DISEASE MECHANISM	DOGS	CATS
Vascular	Ischaemic/haemorrhagic stroke, infrequent	Rare
Inflammatory/infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial, rabies)* Meningoencephalitis of unknown aetiology (GME, necrotizing)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, *Cryptococcus*)* Meningoencephalitis of unknown aetiology (presumed immune mediated); rare
Trauma*	Frequent	Frequent
Toxic*	Frequent	Frequent
Anomalous	Hydrocephalus	Infrequent
Metabolic	Hepatic encephalopathy Hypoglycaemia Hypocalcaemia	Hepatic encephalopathy
Idiopathic	Frequent	Rare
Neoplastic	Infrequent	Infrequent
Nutritional	Thiamine deficiency	Thiamine deficiency
Degenerative	Rare late-onset disease	Rare late-onset disease

* Common cause

Table 38 **Differential diagnosis of seizure activity in patients >6 years old**

DISEASE MECHANISM	DOGS	CATS
Vascular	Ischaemic stroke	Rare
Inflammatory/infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial, rabies)* Meningoencephalitis of unknown aetiology (GME, necrotizing)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, *Cryptococcus*)* Meningoencephalitis of unknown aetiology (presumed immune mediated); rare
Trauma*	Frequent; may be chronic response to earlier trauma	Frequent; may be chronic response to earlier trauma
Toxic*	Frequent	Frequent
Anomalous	Rare	Rare

* Common cause

(Continued)

Table 38 **Differential diagnosis of seizure activity in patients >6 years old** *(continued)*

DISEASE MECHANISM	DOGS	CATS
Metabolic	Hepatic encephalopathy (acquired) Hypoglycaemia (insulinoma*, extrapancreatic insulin-like producing neoplasia, insulin overdose) Polycythaemia	Hypoglycaemia
Idiopathic	Occasional; consider cryptogenic*	Rare; consider cryptogenic
Neoplastic	Primary/metastatic brain tumour*	Primary/metastatic brain tumour*
Nutritional	Rare	Rare
Degenerative	Rare	Rare

* Common cause

DIAGNOSIS OF EPILEPSY AND ITS CAUSES

The importance of the history

Often an owner may describe an event that gives rise to suspicion of an epileptic seizure, but the animal may be normal. It is vital that the clinician asks very specific questions, which will help to determine whether the event could have been a seizure and what the underlying cause may be.

- **Was the first seizure within the past few weeks or months ago?** Extracranial disorders and symptomatic epilepsy may be considered higher on the differential diagnosis list if the seizures began recently. Idiopathic and cryptogenic epilepsy may be more likely in an animal that has had intermittent seizures for many months and is normal in between episodes.
- **Are there signs notable prior to the possible seizure event?** Consistent signs exhibited by the animal prior to the event, such as behavioural abnormalities, are more suggestive of seizures than other possible abnormalities such as narcolepsy or syncope.
- **Describe the event?** Generalized seizures (**132**) are commonly associated with extracranial causes of seizures or inherited epilepsy and are occasionally associated with symptomatic and cryptogenic epilepsy. Focal seizures and focal seizures that generalize secondarily are more often associated with an intracranial disorder such as symptomatic epilepsy or cryptogenic epilepsy. Focal seizures that begin in the facial muscles and then generalize with little motor movement are seemingly more common in cats than in dogs.

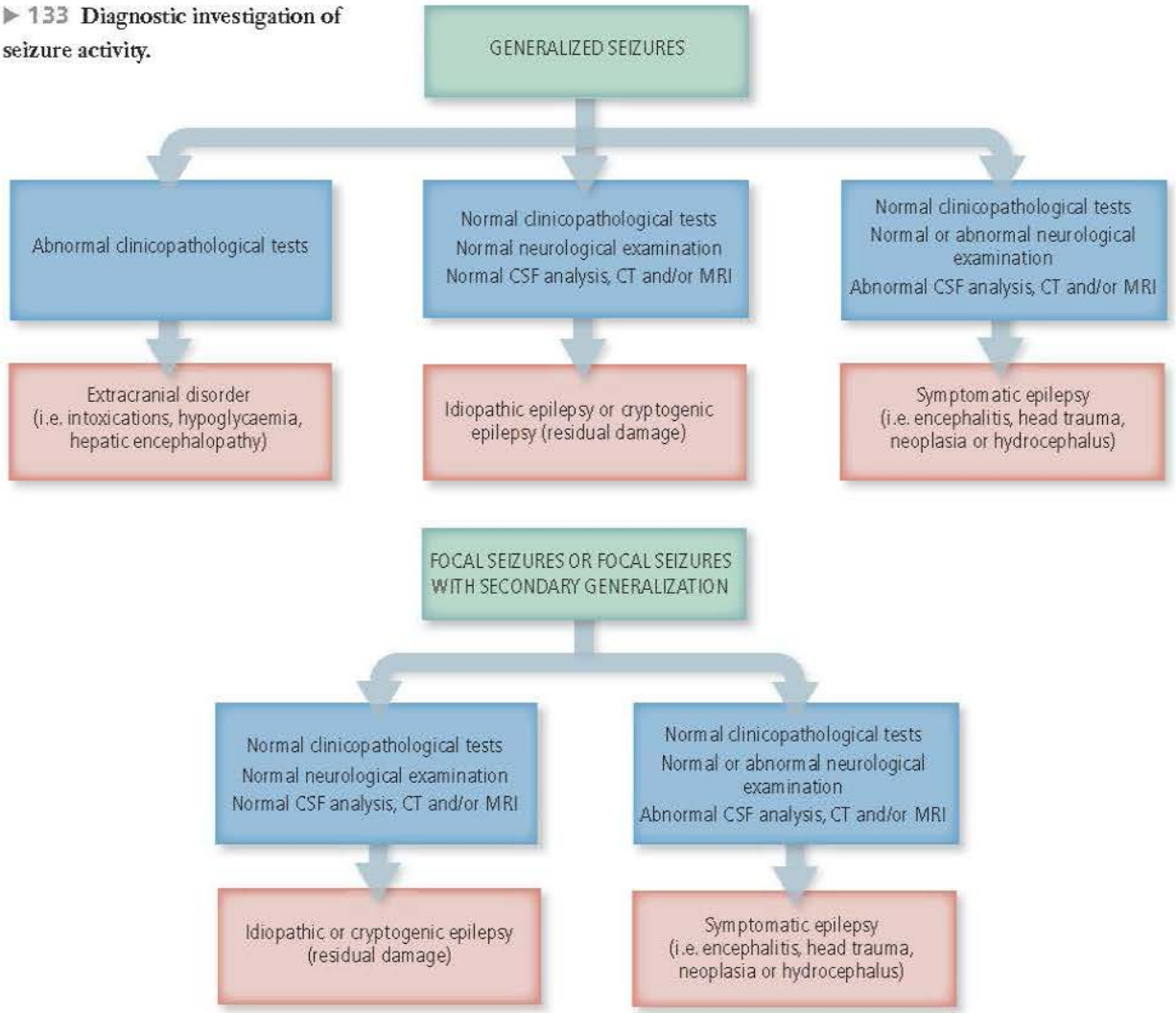


▶ **132** **Generalized seizure activity is often tonic–clonic. The owners should describe evident rigidity in the limbs, as seen in this 10-week-old dog, in addition to involuntary movement.**

Table 39 **Toxins associated with seizure activity in dogs and cats**

TOXIN	CLINICAL SIGNS	ONSET	SPECIFIC ANTIDOTE
Rodenticides			
Alpha-chloralose	Ataxia, seizures, aggression, coma	Acute	None
Bromethalin	Seizures, paralysis	Delayed	None
Strychnine	Seizures	Acute	None
Zinc phosphide	Seizures	Acute	None
Anticoagulants	Rare seizures, rare paralysis	Delayed	Vitamin K1 (2.5 mg/kg PO or SC q24h)
Cholecalciferol	Rare seizures	Delayed	None
Metals			
Lead	Seizure, hysteria, ataxia, tremors, blindness, megoesophagus	Acute if high dose	$CaNa_2$-EDTA (25 mg/kg SC q6h for 5 days)
Thallium	Rare seizures, tremors, ataxia, depression, paresis	Acute	Dithizone (50 mg/kg PO q8h for 5 days)
Organic mercury	Ataxia, hypermetria, tremors, seizures, blindness	Delayed	D-Penicillamine (10–30 mg/kg PO q6h for 1–2 weeks)
Lithium	Tremors, ataxia, coma, seizures	Acute	None
Pesticides			
Insecticides: organosphosphates (OPs) or carbamates	Miosis, salivation, lacrimation, tetany, seizures, coma	Acute	Pralidoxime chloride for neuromuscular signs, but only if OP (20–50 mg/kg IM); atropine for both (0.2 mg/kg IM) if muscarinic signs
Pyrethroids: permethrin, imiprothrin, bifenthrin, allethrin	Hyperexcitability, tremors, seizures	Acute/delayed	None
Molluscicides, metaldehyde	Tachycardia, salivation, tremors, vomiting, hyperaesthesia, nystagmus, ataxia, seizures, hyperthermia, diarrhoea, respiratory failure	Acute	None
Household products			
Ethylene glycol	Depression, seizures, ataxia, coma	Acute	4-Methylpyrazole
Methyelxanthines: caffeine, chocolate, tea	Hyperactivity, ataxia, rare seizures	Acute	None

▶ 133 **Diagnostic investigation of seizure activity.**



- **Seizure length?** Most seizures last a few seconds or minutes. Focal seizures may be brief, but can occur in clusters.
- **Is there any abnormality evident after the possible seizure event?** Identification of a post-ictal phase can be important to confirm seizures, as this activity is not seen with syncope, narcolepsy or REM sleep behaviour disorder. In rare instances the animal may have to be sedated because of prolonged hyperactivity during the post-ictal phase. Occasionally it may become aggressive and should not be handled until this phase resolves.
- **Is the animal normal between the seizures?** If the animal's behavior is abnormal between well spaced seizure events, then seizures from extracranial disorders or symptomatic epilepsy are more likely.
- **Are the seizures associated with sleeping, feeding, fasting, exercise or stressful situations?** Some dogs with idiopathic epilepsy or cryptogenic epilepsy may seizure while sleeping, but cannot be awakened like animals with REM sleep behaviour disorder. Seizures following feeding may be associated with hepatic dysfunction. Seizures during fasting, exercise or stress may be associated with hypoglycaemia. Stressful situations may precipitate seizures in a few dogs with idiopathic or cryptogenic epilepsy.

- **Has there been exposure to other drugs or toxins?** See *Table 39*, page 167.
- **Has the animal been sufficiently vaccinated for the local endemic infections?**
- **Has there been a recent or past illness?**
- **Recent or past head injury?** Seizures may occur at the time of a head injury or up to several years later from residual brain scarring.
- **Is there any familial history of seizures?** If the parents, siblings or other relatives have epilepsy, an inherited problem should be suspected.
- **What is the diet?** Although rare, thiamine deficiency can cause seizures in dogs and cats. Inadequate nutrition leading to hypoglycaemia can cause seizures in toy breed dogs.
- **What previous medications or treatments have been given for seizures?** Current antiepileptic medications or other therapies and their effectiveness should be documented to help develop an effective strategy for long-term seizure management if necessary.

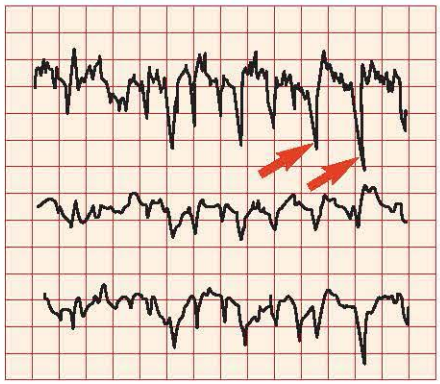
Specific investigations (133)

Suspected extracranial causes

- Complete haematology.
- Comprehensive biochemistry, including pre- and post-prandial bile acids.
- Urinalysis.
- Toxicity screening: serum lead levels; serum cholinesterase levels; 'recreational' drug exposure testing may be available through the local general hospital, or even some pharmacies.
- Infectious disease (IgM and IgG) serology and PCR.

Suspected intracranial causes

- Thoracic radiographs.
- MRI or CT of the brain.
- CSF analysis (protein quantification, complete and differential cell count).
- In those cases with inflammatory CSF or compatible CNS imaging findings, consideration should be give to performing serology/PCR and/or CSF-PCR for all infectious diseases reported in the region/country.



▲ 134 **Electroencephalogram traces from a dog with seizure activity recorded while the dog was under anaesthesia. Multiple spike (arrows) and wave discharges are noted, compatible with abnormal synchronized discharges from multiple cerebrocortical neuronal cells.**

- Electroencephalography can confirm seizure activity in the brain, but is not specific in most cases as to the underlying cause (**134**).

Idiopathic epilepsy

Overview

Idiopathic (inherited) epilepsy has been documented in Beagles, German Shepherd Dogs, Belgian Tervurens, Keeshonds and Dachshunds and is also suspected in Saint Bernards, Australian Shepherd Dogs, Labrador Retrievers, Golden Retrievers, Irish Setters, Standard Poodles, Springer Spaniels, Cocker Spaniels, Lhasa Apsos, Border Collies and many other purebred dogs. Idiopathic epilepsy has not yet been documented in cats.

Clinical presentation

Generalized seizures with loss of consciousness are very common and usually begin at between 1 and 3 years of age, but in a few dogs seizures begin at between 6 months and 1 year of age or between 3 and 7 years of age. The onset of seizures is almost always insidious, beginning with a seizure every few weeks or months, but then becoming progressively more frequent. Many dogs eventually develop cluster seizures or status epilepticus and, in rare cases, this may be the first known seizure activity. German Shepherd Dogs, Australian Shepherd Dogs, Belgian Tervurens, Springer Spaniels, Labrador Retrievers and Saint Bernards are prone to cluster seizures.

Diagnosis

The diagnosis is suspected in a purebred dog with generalized seizures and normal findings on physical and neurological examinations between seizures and all diagnostic tests including MRI and CSF analysis. Breeding trials may be needed to confirm the diagnosis if no other dogs in the lineage have had seizures. Unless animals are presented with severe cluster seizures or status epilepticus, therapy is aimed at controlling the seizures with maintenance anticonvulsant therapy.

It would not be unreasonable to make a diagnosis of idiopathic epilepsy in a dog (and to a lesser extent a cat) demonstrating:

- The right age and signalment (particularly in a breed with a high incidence of idiopathic epilepsy).
- A normal haematological and biochemical evaluation.
- History and seizure characteristics consistent with idiopathic epilepsy (generalized tonic–clonic seizures from rest and with the seizure onset at between 1 and 3 years of age). (*Note:* From 6 months to 6 years is acceptable.)
- No abnormalities in the inter-ictal period.
- If these cases later develop additional clinical signs to suggest an alternative diagnosis or if the seizure control is poor, then further investigation would be justified.

Management

The treatment of seizure activity on an emergency basis is detailed in Chapter 23. Unless idiopathic or cryptogenic epilepsy is considered to be the primary differential for the seizure activity, specific treatment of the underlying cause is essential and the success of this will determine the need for symptomatic seizure therapy.

The aims of seizure treatment are:

- To reduce the frequency and severity of seizures. (It is important to explain to the owner that the animal may still seizure despite the therapy.)
- To minimize potential side-effects.
- To maximize the owner's and dog's quality of life.

Table 40 **Maintenance anti-epileptics for use in cats**

DRUG	$T_{1/2}$ (hours)	RECOMMENDED DOSE	MAJOR POSSIBLE SIDE-EFFECTS
Phenobarbitone	34–43	2–5 mg/kg/day PO (divided q12h)	Sedation; ataxia; polyphagia with weight gain; thrombocytopenia; swelling of feet; facial pruritis; cutaneous eruption; lymphadenopathy
Diazepam	15–20	0.5–2.0 mg/kg/day PO (divided q12h or q8h)	Acute hepatic necrosis; sedation; ataxia
Potassium bromide	10 days	30 mg/kg/PO q24h	Bronchial asthma
Gabapentin		5–10 mg/kg PO q24h	Sedation; ataxia
Levetiracetam	3	10–20 mg/kg PO q8h	Sedation; decreased appetite
Zonisamide	33–35	5–10 mg/kg PO q24h	Sedation; anorexia; vomiting; diarrhoea
Pregabalin		5–10 mg/kg PO q12h	Sedation

(Modified from Podell M (2005) Seizures. In: *BSAVA Manual of Canine and Feline Neurology*. (eds. SR Platt, NJ Oldby) British Small Animal Veterinary Association, Gloucester.)

Table 41 **Maintenance anti-epileptics for use in dogs**

DRUG	$T_{1/2}$ (hours)	TSS (days)	SUGGESTED SERUM THERAPEUTIC RANGE	RECOMMENDED DOSE	POSSIBLE SIDE-EFFECTS
Phenobarbitone	32–89	10–18	20–35 mg/dl	2–3 mg/kg PO q12h	Sedation; ataxia; polydipsia/polyuria; polyphagia; hyper-excitability; hepatotoxicity; induces P450 system; bone marrow dyscrasia; pancreatitis
Potassium bromide	21–24 days	2.5–3.0 months	1–3 mg/ml	20–40 mg/kg PO q24h	Sedation; weakness; polydipsia/poyuria; polyphagia; pancreatitis; pruritis; behavioural changes
Felbamate	5–6	1–2	25–100 mg/l	15–70 mg/kg PO q8h	Blood dyscrasias; liver disease; dry eye
Topiramate	20–30	3–5	2–25 mg/l	2–10 mg/kg PO q12h	Vomiting; diarrhoea; sedation
Clorazepate	5–6	1–2	20–70 µg/l (nordiazepam)	0.5–1.0 mg/kg PO q8–2h	Sedation
Zonisamide	15–20	3–4	10–40 µg/ml	2.5–10.0 mg/kg PO q12h	Sedation; loss of appetite; dry eye; ataxia
Gabapentin	3–4	1	4–16 mg/l	10–20 mg/kg PO q8h	Sedation; ataxia
Levetiracetam	3–4	1	Not known	10–20 mg/kg PO q8h	Sedation; ataxia
Pregabalin	7	2–3	>2.8 µg/ml	3–4 mg/kg PO q8h–12h	Sedation; ataxia

TSS = approximate time to steady state

(Modified from Podell M (2005) Seizures. In: *BSAVA Manual of Canine and Feline Neurology*. (eds. SR Platt, NJ Oldby) British Small Animal Veterinary Association, Gloucester.)

Although largely arbitrary and greatly dependent on owner demands and compliance, the following would be a reasonable guide as to when to start treating seizures:

- When more than one seizure occurs per month and/or the owners object to their frequency.
- If the animal has a very severe seizure or cluster of seizures, irrespective of the frequency of the seizures or seizure clusters.
- The seizures are increasing in frequency or severity.
- An underlying progressive intracranial disorder has been identified as the cause of the seizures.
- Post-ictal signs are objectionable (e.g. aggression).

Specific drugs for seizure treatment in cats and dogs can be found in *Tables 40* and *41*, respectively.

EXERCISE-ASSOCIATED WEAKNESS AND COLLAPSE

Arianna Negrin & Simon Platt

INTRODUCTION

Exercise- or activity-associated weakness and collapse and exercise intolerance are distinct entities. They may represent different clinical expressions of a primary neuromuscular (NM) disease or can be secondary to cardiovascular, metabolic/systemic or primary CNS conditions, including narcolepsy/cataplexy.

The NM system is composed of motor units, consisting of the neuronal cell body situated in the ventral horn of the spinal cord, its axon, the NM junction and the muscle unit composed of muscles fibres. In addition to motor units, there is a sensory component existing as receptors, peripheral sensory axons, which are associated with motor axons in most nerves, and dorsal root ganglions. The NM system has been referred to as the LMN system and in this chapter the two terms will be considered synonymous.

In the clinical approach to the weak patient, it is important to define the specific terminology used:

- **Weakness**, or paresis, is the inability to generate voluntary movement and/or to support weight due to a lesion affecting the upper or lower motor pathway. Signs of NM weakness relate to a lesion of the LMN pathway. They include flaccid paresis/paralysis, often manifested as a short-strided gait and a progressive reluctance to walk or run. Additional signs accompanying NM weakness include ventroflexion of the neck, hyperflexion of the joints, a plantigrade posture, a generalized decrease in muscle tone, occasional muscle tremors and, in chronic cases, muscle atrophy.
- **Collapse** is an acute event that may be a manifestation of more chronic and progressive NM diseases; however, it is important to consider the three major differential diagnoses of collapse in addition to NM disease: seizures, syncope and narcolepsy–cataplexy. Metabolic diseases (including Addisonian crisis) and paroxysmal disorders (i.e. Scotty cramp/Cavalier King Charles Spaniel hypertonicity/sleep disorders) also need to be considered as differentials in the collapsed patient.
- **Exercise intolerance** can be considered as intermittent weakness or collapse, associated with different levels of activity, which improves with rest. Respiratory and cardiovascular dysfunction, as well as orthopaedic disease, need to be considered as a potential cause of exercise intolerance in addition to those diseases responsible for collapse.
- **Narcolepsy** and **cataplexy** are disorders in sleep/wake control that may cause acute weakness, sometimes associated with physical activity. Narcolepsy, defined as excessive daytime sleepiness with alteration of nocturnal sleep patterns, has been reported in many canine breeds and in some of them (Labrador Retrievers and Doberman Pinschers) an autosomal recessive inheritance has been demonstrated. Cataplexy is characterized by sudden flaccid muscular weakness, ranging from dropping of the jaw or head to complete collapse without loss of consciousness, frequently induced by excitement, such as eating or playing, and often manifesting as muscular weakness (see Chapter 6). The pathophysiology is still unclear; however, recent studies have suggested that deficiency of some hypothalamic neuropeptides (hypocretins) and/or their receptors may play an important role in the development of these sleep disorders.

Table 42 **Key questions regarding episodic weakness, collapse or paroxysmal events**

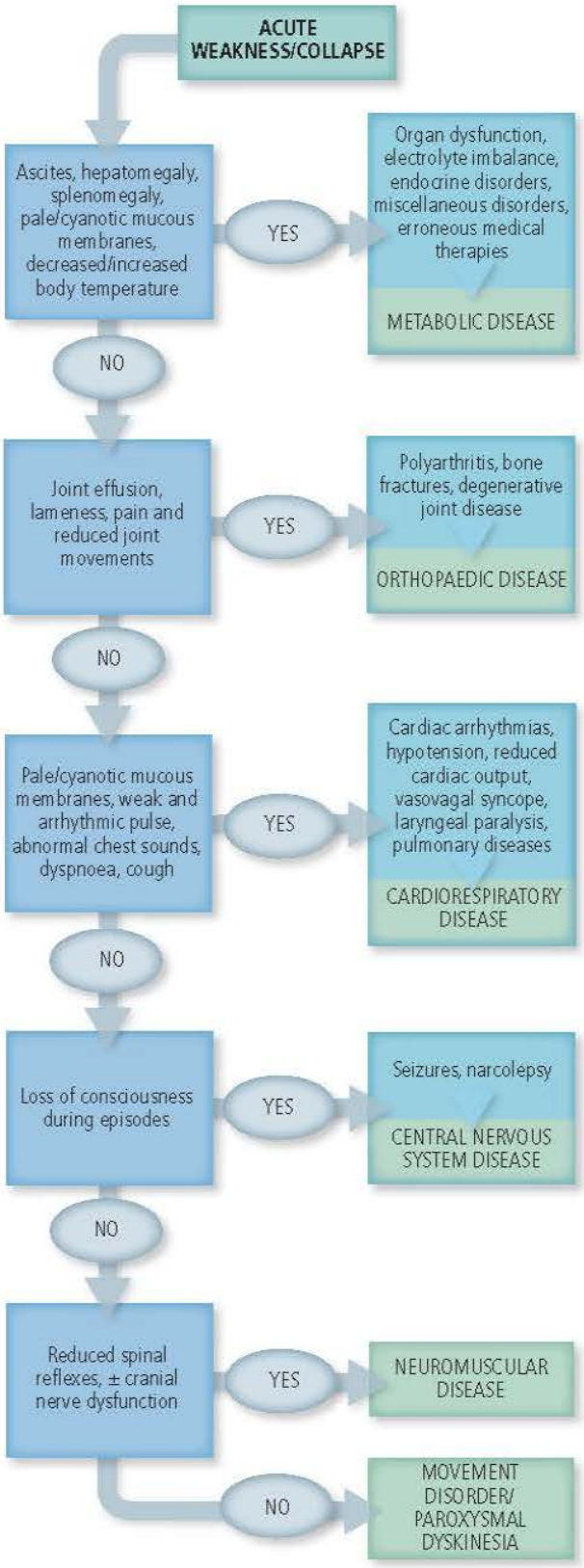
QUESTION	IMPLICATIONS
What did the event look like?	It may be difficult to distinguish the event from seizure activity, and some may be seizures, but it will be important to establish that these events are not due to a metabolic or cardiovascular crisis
Has this happened before?	Episodic or paroxysmal events that warrant investigation should be recurrent
How often has this happened?	The answer will provide an insight into the progressive nature of the disease and will serve as a marker for response to therapy
Has it always had the same characteristics?	Paroxysmal events are usually stereotypical
Is the animal 'normal' immediately after these events?	A seizure may be followed by a period of confusion, visual dysfunction, compulsion or even aggression. NM disorders, movement disorders and syncopal events usually have no such associations
Is there any type of trigger factor that can be identified?	Excitement or eating, which often causes a loss of consciousness and/or collapse, should prompt the thought of narcolepsy/cataplexy. Several documented events occur during sleep, such as the REM sleep disorder. Exercise/excitement may be the trigger for the syndromes described in Cavaliers and Scotties as well as many NM diseases and hypoglycaemic-related collapse. Rarely, seizure events will be triggered by a specific noise or action. Events seen more than 8 hours after last feeding may suggest hypoglycaemic collapse
Is the animal normal in between the events?	Any abnormalities described in between the episodes could indicate a structural CNS or neuropathic or myopathic disease. Metabolic and cardiovascular diseases may be associated with a waxing and waning clinical course, with some abnormalities detectable in between the acute events
Are any other littermates known to be affected?	Breed-associated events may be seen in related siblings; however, underlying infectious diseases and toxicities should not be ignored
Is the animal stiff or floppy at the time of the event?	Stiffness at the time of the event would often imply either a seizure event, a movement disorder or a myopathy. A floppy animal at the time of the event could also be a myopathy, but could also indicate a cardiovascular or metabolic disease
Are the gums pale at the time of the event?	Mucous membrane pallor could well indicate a cardiovascular disease; however, metabolic diseases, such as Addison's disease, should also be considered

- **Paroxysmal breed related disorders** (Scotty cramps, hypertonicity in Cavalier King Charles Spaniels, paroxysmal dyskinesia in Chinooks and 'cramping' in Norwich Terriers) are characterized by sudden and transient onset of neurological signs often elicited by stress or exercise and most likely due to abnormal CNS neurotransmission. The neurological scenario is usually characterized by initial progressive stiffness of the forelimbs, followed by the hindlimbs, and it may progress to recumbency without loss of consciousness. These episodes usually resolve spontaneously within 10 minutes (see Chapter 13).

The approach to a patient with acute exercise- or activity-associated weakness or collapse may be very challenging for the clinician, as numerous aetiologies can potentially be responsible. A complete physical and neurological examination, combined with the information on the signalment and anamnesis, represents the first and one of the most important steps in deciding if the weakness/collapse originates from a primary neurological condition (including NM or CNS diseases) or is caused by cardiovascular, respiratory, metabolic or orthopaedic disorders (*Table 42*).

The main differential diagnoses for neurological causes of exercise- or activity-associated weakness/collapse depend on the lesion localization (i.e. CNS and the three main subdivisions of the NM system: neuropathies, junctionopathies and myopathies).

The systemic causes of exercise- or activity-associated weakness or collapse, such as orthopaedic, metabolic and cardiorespiratory conditions, should be ruled out prior to investigating the NM system (**135**). Most metabolic disorders may have an effect on the functions of other systems, including the NM system and CNS, creating a complex mixture of clinical signs. For this reason, evaluation of the real neurological component of weakness in these animals may be very difficult or, sometimes, impossible until the metabolic imbalance has been addressed.



▶ **135** **Systemic approach to an acutely collapsing animal.**

- **Step 1.** Rule out orthopaedic diseases, including polyarthritis, degenerative joint disease, developmental bone disorders and bone fractures. Physical examination may detect a stiff gait associated with joint effusion and pain in dogs with polyarthritis; this can be confirmed by synovial fluid analysis and joint radiographs (**136**). Radiographs are useful in the detection of appendicular bone fractures, developmental bone disorders (panosteitis, metaphyseal osteopathy) and in degenerative arthropathies. Blood tests, serology for infectious agents (*Ehrlichia* spp., *Borrelia burgdorferi*, *Mycoplasma* spp., FeLV), synovial fluid culture and an antinuclear antibody test are some of the tests often required to investigate the aetiology of polyarthritis.
- **Step 2.** Rule out metabolic diseases, including electrolyte imbalance, endocrine diseases (addisonian crisis, insulinoma, hypoglycaemia, diabetic ketoacidosis), erroneous dosage of treatments (insulin) and miscellaneous disorders (anaemia, shock, acidosis, pyrexia). Physical examination may detect signs of ascites, weak peripheral pulses, bradycardia, hepatomegaly, splenomegaly, pale/cyanotic mucous membranes, decreased/increased body temperature and vomiting/diarrhoea. Diagnosis may be reached through the use of multiple standard diagnostic tests (see Specific diagnostic tests, p. 184).
- **Step 3.** Rule out cardiorespiratory diseases, including arrhythmia, hypotension, reduced cardiac output, vasovagal syncope, thromboembolism, laryngeal paralysis, pulmonary disease and pleural/pericardial effusion. Pale/cyanotic mucous membranes, weak and irregular pulse, abnormal chest sounds, dyspnoea and coughing should alert the clinician to investigate the potential for cardiorespiratory diseases. Chest radiographs, ECG and echocardiography are mandatory in every patient with a history of collapse and signs of cardiorespiratory disease.
- **Step 4.** Rule out CNS disorders, including seizures, narcolepsy and paroxysmal movement disorders. CNS lesions may cause a sudden generalized collapse/weakness with a loss of consciousness and may be associated with excitement or exercise. CNS lesions may be associated with visual deficits, abnormal behaviour and/or levels of consciousness as well as CN deficits. Sometimes, history, signalment and clinical examination may not help rule out a CNS lesion or related event and so the clinician needs to rely on diagnostic tests, video footage provided by the owner and treatment trials.

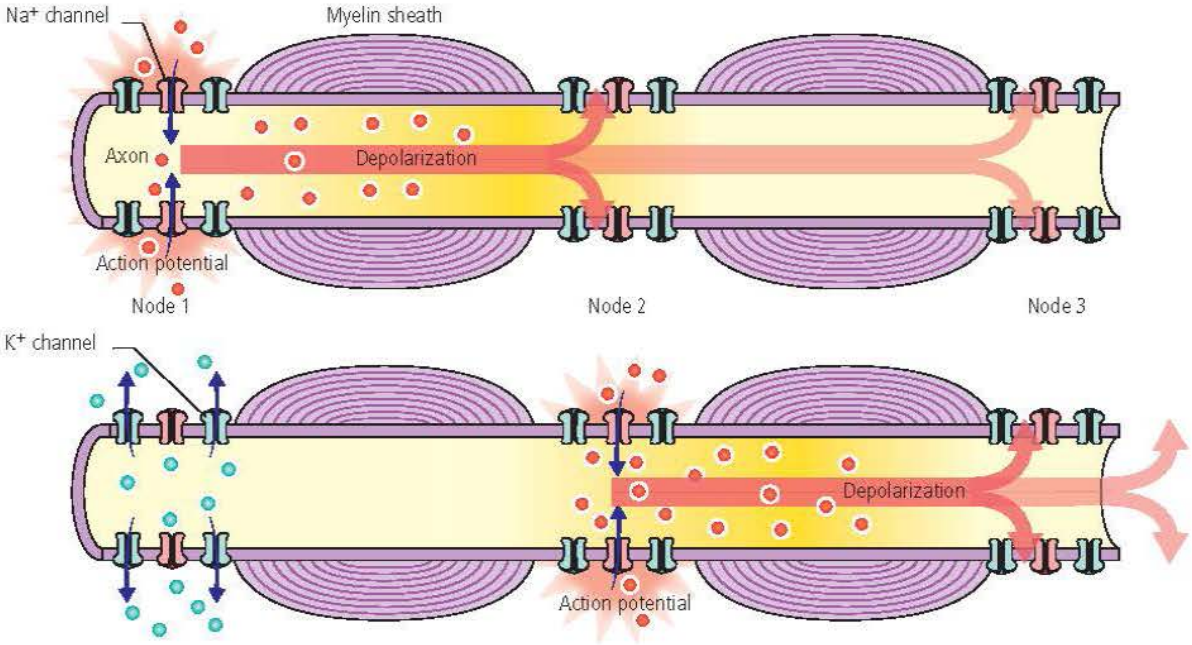


▲ **136** Lateral carpal radiograph of a dog that exhibited weakness due to polyarthritis. Soft tissue swelling and periosteal proliferation are evident.

NEUROANATOMICAL BASIS OF NEUROMUSCULAR CAUSES OF WEAKNESS AND COLLAPSE

Knowledge of the basic physiology of nerve and muscle function is essential for comprehending their dysfunction. The physiology of the NM system can be divided into two main areas:

- **Ion function.** Ions such as sodium, potassium and calcium are essential for impulse generation and transmission and for the mechanism of muscle contraction.
- **Energy metabolism of myofibres.** Normal energy reserves and metabolism are required for adequate muscle contraction and relaxation.

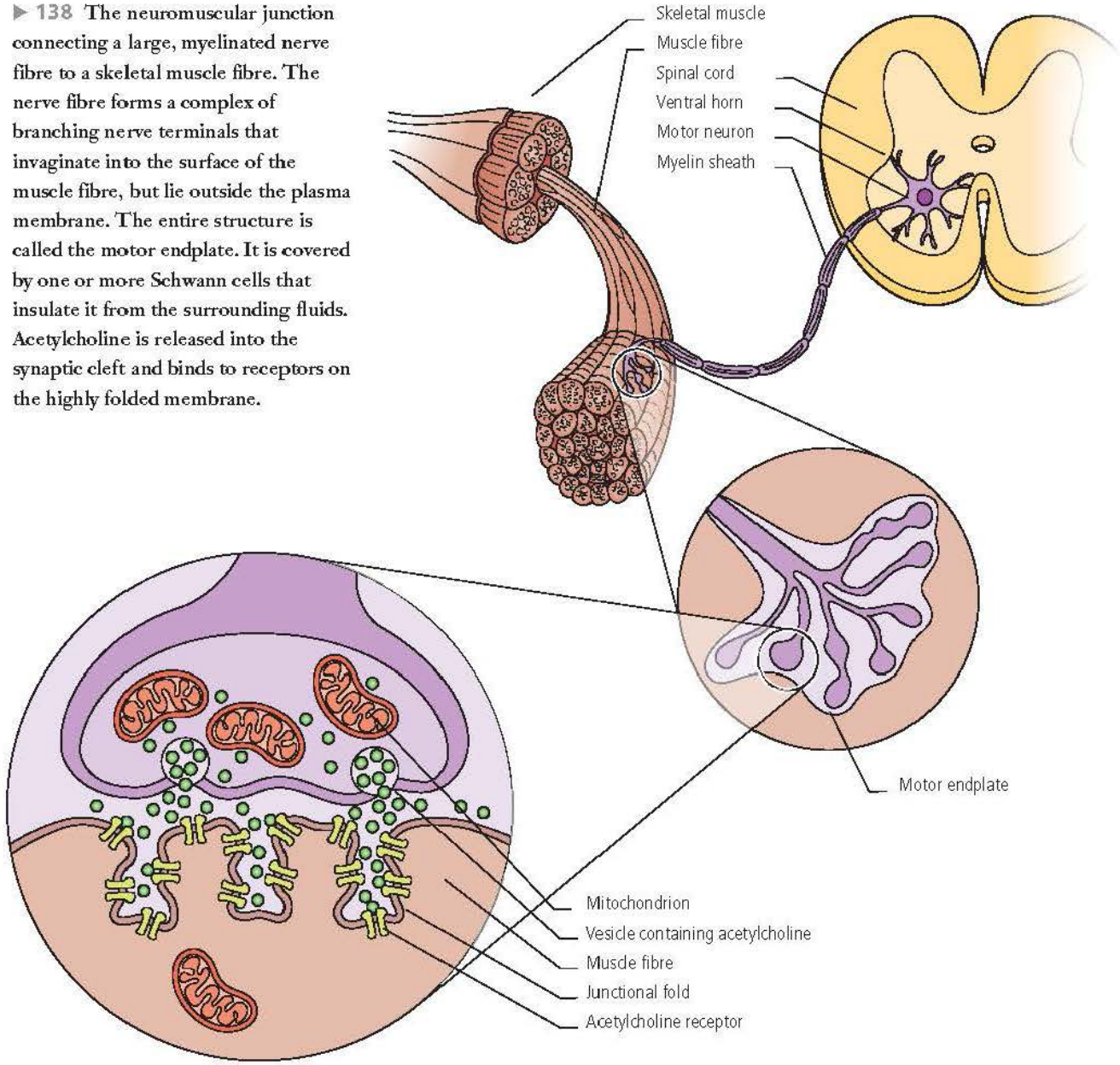


▲ **137** **Saltatory conduction is the mechanism by which signals travel in myelinated nerves. As sodium ion channels open at the unmyelinated nodes of Ranvier, that section of the membrane is depolarized, resulting in an action potential that is conducted from node to node as subsequent channels are triggered. Electrical current flows through the surrounding extracellular fluid outside the myelin sheath, as well as through the axoplasm inside the axon.**

Ion function

Normal skeletal muscle fibres are stimulated by the LMN via the creation of electrical action potentials generated at the NM junction (motor endplate). A presynaptic action potential is generated by movement of sodium and potassium ions along the nerve-cell membrane and is influenced by calcium. An electrical potential exists in all cells, called the membrane potential (resting potential), whereby the inside of the cell is negatively, and the outside is positively, charged. The membrane potential of nerve and muscle cells is capable of abrupt change into an action potential providing a capacity for 'excitement'. In the resting state, sodium concentration is high outside the nerve cell (in the extracellular fluid), while potassium concentration is high inside the cell (intracellular compartment); this is regulated by the sodium–potassium pump, which exchanges 3 sodium ions for 2 potassium ions, leaving a net deficit of positive ions on the inside and maintaining a stable membrane potential at -70 mV. Nerve signals are transmitted by action potentials, which are rapid changes to a positive potential (depolarization) with a rapid return to a negative potential (repolarization). During depolarization the cell membrane becomes very permeable to sodium ions, allowing a large number of sodium ions to diffuse into the interior of the axon, with an increase in the membrane potential (depolarization). Once the potential attains positivity (+35 mV), the sodium channels begin to close and potassium ions diffuse to the exterior, re-establishing the normal negative resting membrane potential (repolarization) (see **125**). The axon is surrounded by a myelin sheath; every 1–3 mm along the length of the myelin sheath is a node of Ranvier. This is a junction between two Schwann cells, which form the myelin around the axon. The depolarization process travels along the entire nerve from node to node to the NM junction (motor endplate); this is termed saltatory conduction (**137**).

▶ **138** **The neuromuscular junction connecting a large, myelinated nerve fibre to a skeletal muscle fibre. The nerve fibre forms a complex of branching nerve terminals that invaginate into the surface of the muscle fibre, but lie outside the plasma membrane. The entire structure is called the motor endplate. It is covered by one or more Schwann cells that insulate it from the surrounding fluids. Acetylcholine is released into the synaptic cleft and binds to receptors on the highly folded membrane.**



The nerve-fibre terminals invaginate into the surface of the myofibres, forming a structure called the motor endplate or NM junction (**138**). The space in between the muscle membrane (postsynaptic membrane) and the nerve fibre membrane (presynaptic membrane) is called synaptic space and it represents the site where transmission of impulses between nerve and muscle takes place, mediated by the neurotransmitter acetylcholine (ACh).

When an action potential spreads over the terminal of the nerve fibre, voltage-gated calcium channels open, allowing calcium ions to diffuse from the synaptic space into the nerve terminal. The calcium ions serve to modulate the subsequent release of ACh at the motor endplate, stimulating ACh vesicles to fuse with the neural membrane.

Activation of ACh-gated ion channels in the muscle-fibre membrane allows large numbers of positive ions (Na^+, K^+ and Ca^{++}), in particular sodium ions, to diffuse inside the myofibre, creating a local positively-charged potential, called an endplate potential, which secondarily spreads along the muscle membrane. Once ACh is released into the synaptic space it is rapidly removed by acetylcholinesterase, an enzyme that degrades ACh, thus avoiding continuous stimulation of the post-synaptic membrane.

Once depolarization reaches the muscle fibre, the sarcoplasmic reticulum releases large quantities of stored calcium ions, which become responsible for myofibre contraction and subsequent relaxation. In summary, ionic imbalances, particularly of calcium or potassium, may produce severe alterations of nerve and muscle function, resulting in episodic weakness.

Energy metabolism

Contraction of myofibres essentially requires energy. Two main substrates supply energy to the muscle: glycogen and fatty acids, through glycolysis and β-oxidation, respectively. During intense exercise the primary source of energy for muscle is glycogen via anaerobic glycolysis, in which glycogen is converted to pyruvate, which is transported to mitochondria where it is incorporated into the tricarboxylic acid (TCA) cycle for energy production.

Lipids, on the other hand, in the form of fatty acids, are the major substrates for energy production during aerobic muscle contraction via mitochondrial β-oxidation during sustained exercise. Carnitine plays a major role in modulating transport of fatty acids into mitochondria for β-oxidation; it also acts as a buffer against accumulation of organic acids, transferring them outside the mitochondria to be excreted in the urine.

Therefore, disorders of muscle metabolism can cause acute weakness associated with exercise.

Table 43 **Electrolyte abnormalities and neuromuscular weakness**

ABNORMALITY	PRIMARY CAUSES	CLINICAL SIGNS
Hyperkalaemia	Acute renal failure Hypoadrenocorticism K^+ sparing diuretics Metabolic acidosis Iatrogenic	Muscle weakness Cardiac arrhythmia
Hypokalaemia	Renal loss Intestinal loss Metabolic alkalosis	Muscle weakness Hypovolaemia
Hypocalcaemia	Primary hypo-parathyroidism Hyperphosphataemia Eclampsia Iatrogenic	Muscle weakness Tetany Mental depression Seizures
Hypercalcaemia	Malignant tumours Primary hyper-parathyroidism Hypervitaminosis D	Muscle weakness Mental depression Polydipsia/polyuria Constipation
Hyponatraemia	Intestinal loss Hypoadrenocorticism Inappropriate anti-diuretic hormone secretion Iatrogenic	Muscle weakness Lethargy Seizures Coma
Hypernatraemia	Water deprivation Excess salt gain Pure water loss	Muscle weakness Muscle rigidity Tremors Seizures Coma

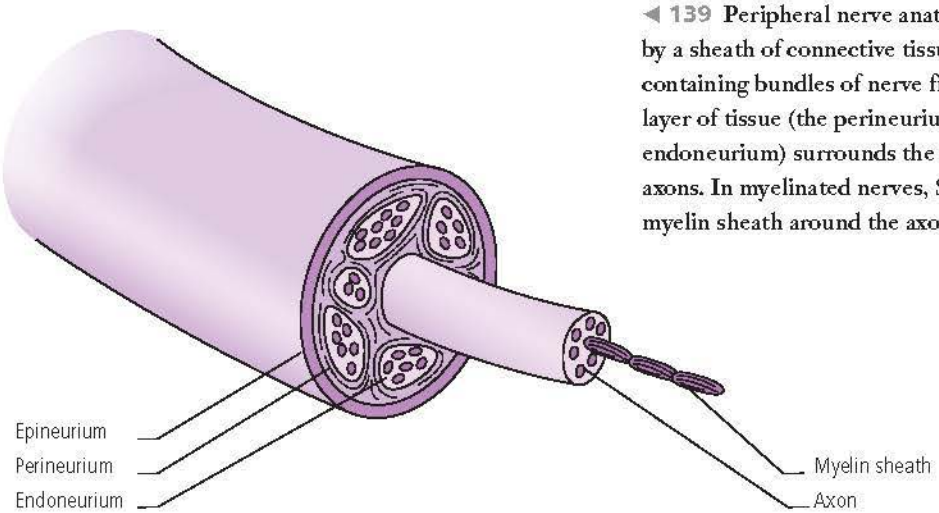
Neuromuscular system causes of weakness and collapse

Potential NM abnormalities causing acute generalized weakness/collapse can be due to dysfunction at one of the three levels into which the NM system is functionally divided: nerve transmission (neuropathies); NM transmission (junctionopathies); and muscle contraction (myopathies). Ion disorders mainly affect nerve and NM junction transmission, while muscle contraction depends highly on energy metabolism. However, ionic balance, especially between calcium and potassium, is also essential in normal muscle contraction, and electrolyte abnormalities are associated with a wide range of signs (*Table 43*).

In nerve transmission, disorders affecting the axon structure (**139**) or the myelin organization affect the velocity and/or amplitude of action potentials transmitted along the nerve fibre, resulting in muscular weakness. The clinical signs and differential diagnosis of a peripheral neuropathy are listed in *Tables 44* and *45*, respectively.

The major NM junction abnormalities causing acute collapse are ion disorders, altered ACh release (botulism, tick paralysis) or degradation (OP/carbamate toxicity) and ACh receptor dysfunction (congenital or acquired MG). A complete differential diagnosis for NM junction disease in dogs and cats affected by exercise- or activity-associated acute weakness and collapse is listed in *Table 46*.

Efficient muscle contraction requires ionic balance (in particular between potassium and calcium ions), intact myofibre structure and contraction coupling, and efficient energy metabolism. The clinical signs and differential diagnosis of myopathy are detailed in *Tables 44* and *47*, respectively.



◀ **139 Peripheral nerve anatomy. Each nerve is covered by a sheath of connective tissue (the epineurium) containing bundles of nerve fibres wrapped in a second layer of tissue (the perineurium) while a further layer (the endoneurium) surrounds the individual nerve fibres or axons. In myelinated nerves, Schwann cells create a myelin sheath around the axons.**

Table 44 Differentiation of neuropathy from myopathy on the neurological examination

	PERIPHERAL NEUROPATHY	MYOPATHY
Mental status	Normal	Normal
Posture/gait	Plantigrade stance; flaccid paresis or paralysis; ataxia may be present if the sensory nerve is affected (rare)	Stiff and paretic gait; exercise-induced weakness/stiffness
Postural reactions	Decreased (sensory)	Decreased only in severe weakness
Cranial nerves	May be involved	Rarely affected
Spinal reflexes	Decreased to absent	Decreased only in chronic muscle disease
Muscle tone	Decreased (motor)	Normal to decreased (rarely increased)
Sensation	Decreased to absent unless pure motor nerve disease	Normal
Muscle atrophy	Present; often severe and rapid in onset and progression	Atrophy or hypertrophy; muscle contracture may be present in chronic cases

Table 45 **Differential diagnosis for exercise-associated weakness and collapse due to peripheral nerve disease**

DISEASE MECHANISM	EXAMPLES
Vascular	Ischaemic neuromyopathy (see note) Vascular anomalies compressing the nerve roots (rare)
Inflammatory/infectious	Acute idiopathic polyradiculoneuritis* Infectious polyneuropathies (*Neospora caninum*, feline leukaemia virus, feline immunodeficiency virus) Brachial plexus neuritis
Toxic	Toxic/drug-induced neuritis (vincristine, organophosphates)
Metabolic	Diabetes mellitus (D, C) Hypothyroidism (D)* Electrolyte imbalance* (see *Table 43*) Hypoglycaemia-associated neuropathy
Idiopathic	Distal denervating disease
Neoplastic	Neoplastic (lymphoma, peripheral nerve sheath tumour, malignant sarcoma) Paraneoplastic immune-mediated polyneuropathy (insulinoma, lymphoma, pulmonary carcinoma, haemangiosarcoma)

* Common cause; D = dog; C = cat.

Note: Ischaemic neuromyopathy usually affects the hindlimbs and is characterized by acute onset and static progression, but can infrequently be exercise/activity related and intermittent. It is important to assess peripheral pulses and abdominal vasculature in dogs and cats presented with intermittent weakness.

NEUROLOGICAL EVALUATION

In a patient with activity-associated weakness or collapse and where a neurological condition is suspected rather than abnormalities of other systems, a detailed history (see *Table 42*) and neurological examination are mandatory. A thorough description of the weakness or collapse, especially if supported by video footage, can provide important information about the speed of onset of neurological signs, potential loss of consciousness during the events and type of activity the patient was performing at the time of the 'episode'.

The neurological examination aims to localize the lesion within the nervous system in order to list appropriate differential diagnoses and establish what further tests might be necessary.

Table 46 **Differential diagnosis for exercise-associated weakness and collapse due to disorders of the neuromuscular junction**

DISEASE MECHANISM	EXAMPLES
Toxic	Botulism* Tick paralysis* Organophosphate/carbamate toxicity Snake bite
Anomalous	Congenital myasthenia gravis*
Idiopathic	Acquired myasthenia gravis*
Neoplastic	Paraneoplastic myasthenia gravis

* Common cause

Table 47 Differential diagnosis for exercise-associated weakness and collapse due to disorders of the muscles

DISEASE MECHANISM	EXAMPLES
Vascular	Ischaemic neuromyopathy (see note)
Inflammatory/infectious	Immune-mediated inflammatory myopathies (D)* Infectious polymyositis* (*Toxoplasma gondii, Neospora caninum*), (*Ehrlichia* spp., bacterial, very rare)
Metabolic	Diabetic ketoacidosis (hypokalaemic myopathy in cats)* Hypothyroidism (D)* Hyperthyroidism (C)* Hyperadrenocorticism* Hypoadrenocorticism (D)* Electrolyte imbalance (see *Table 43*) (hypokalaemic myopathy in cats)* Hypoglycaemia (D, C)* Myopathy related to glucocorticoid excess Heat stroke rhabdomyolysis (D, C) Mitochondrial myopathy (D) Lipid storage myopathy (D)
Idiopathic	Exertional rhabdomyolysis (D) Breed specific exercise-induced collapse (D) Necrotizing polymyositis (D)
Neoplastic	Neoplastic (lymphoma, peripheral nerve sheath tumour, rhabdomyosarcoma, metastatic neoplasia) Paraneoplastic polymyositis (lymphoma)
Nutritional	Vitamin E deficiency (D)

* Common cause

D = dog; C = cat.

Note: Ischaemic neuromyopathy usually affects the hindlimbs and is characterized by an acute onset and static disease, but it can infrequently be exercise/activity related and intermittent.

Activity-associated weakness is the most typical clinical sign of NM disease. Interpretation of the neurological examination may be challenging in these patients. At the time of examination they may appear normal or only mildly affected; additionally, if weakness is exhibited, it is rarely specifically indicative of nerve, NM junction or muscle disease. In a patient with a NM disorder, observation and gait analysis may detect ventroflexion of the neck, a short-strided gait with overflexion of the joints (often more evident in the hindlimbs), a plantigrade stance at rest (**140**) and a generalized decreased muscle tone. In general:

- In contrast to UMN diseases, disorders of the LMN do not cause ataxia, only paresis. Due to their close anatomical relationship within the caudal brainstem and spinal cord, most gait abnormalities involving the UMN pathways necessary for gait generation also cause some degree of proprioceptive ataxia. Diseases affecting the LMN system are, by definition, not ataxic. If ataxia is present in the collapsing patient, a lesion affecting the cerebellum, the vestibular system or the ascending general proprioceptive pathways in the spinal cord should be considered.
- NM disease can be asymmetrical in presentation.
- The hindlimbs can be affected without obvious signs in the forelimbs in patients with acute-onset NM disease.



▲ **140** **A plantigrade stance suggestive of peripheral nerve disease.**

A neurological evaluation should follow the following steps:

- **Step 1.** Confirm the exercise/activity relationship to the problem described. Exercise testing is mandatory and represents a good tool in evaluating metabolic pathways. From rest to maximal exercise, energy demand progressively exacerbates clinical signs due to the increased muscle metabolism. The relationship of the primary complaint to activity may be obvious in some patients after a few steps, but in some it may require a few minutes of activity to assess the potential effects on the gait. This is obviously very difficult in the cat. A protracted period of observation may be essential in a room where the cat cannot seek a hiding place. The main purpose of this step is to further confirm the suspicion of a peripheral neurological abnormality by determining whether the characteristics of the gait are compatible with NM disease. Additionally, this will give the observer a chance to assess the severity of the problem, the onset of pain with activity (which may not be present at rest) and the effects of activity on the cardiorespiratory system.
- **Step 2.** Is the lesion UMN or LMN? Once a neurological abnormality has been observed, the paresis must be determined to be either UMN or LMN in origin, although spinal localization is very unlikely for neurological presentation exacerbated by or exclusively present at exercise. Disorders of the UMN system result in spastic paresis and normal to increased spinal reflexes, while NM conditions (LMN system disorders) are characterized by flaccid paresis and decreased spinal reflexes. However, many NM conditions may actually manifest with an apparent increase in tone, or stiffness, at the time of the exercise- or activity-associated weakness or collapse. Segmental spinal reflexes should be evaluated before and after exercise or activity.
- **Step 3.** Is the disease focal versus diffuse? In a patient affected by generalized weakness associated with exercise intolerance, the neurological examination should aim to detect any other peripheral nerve dysfunctions. Diffuse NM disease often causes the spinal reflexes in all limbs to be reduced to absent. In more generalized NM diseases, specific dysfunctions, such as dysphagia (pharyngeal paralysis), dysphonia (laryngeal paralysis), regurgitation (oesophageal abnormalities) and extraocular muscle paresis, as well as intercostal and diaphragmatic muscle weakness, may be observed. Focal LMN disease may represent early-onset disease, especially in the acute stages, with the potential for rapid deterioration, but it may also represent a focal lesion in the spinal cord affecting the cell bodies of the LMNs.
- **Step 4.** Is the disease affecting peripheral nerve, muscle or NM junction? From a clinical point of view, in the majority of cases, distinguishing a neuropathy from a junctionopathy or a myopathy is not possible. However, some parts of the neurological examination, including evaluation of gait, postural reactions, spinal reflexes and sensation, can be particularly helpful in distinguishing a muscular from a peripheral nerve disorder (see *Table 44*). In summary:
  - Postural reaction deficits (knuckling) are usually only present with peripheral nerve problems and not NM junction and muscle disease. However, it may be difficult to evaluate very weak patients and to discern whether the postural reaction abnormalities are real or not.



▲ **141** **Profound muscle atrophy in the muscles supplied by the sciatic nerve suggests neurogenic atrophy.**

- The flexor withdrawal reflex is usually intact with NM junction disease and acute-onset muscle disease, but multiple rapid repetition may cause its progressive decrease. These reflexes are often reduced with peripheral nerve disease and with chronic muscle disease.
- Muscle atrophy will be seen with nerve and muscle disease after 7–10 days, but not with NM junction disease (**141**).

Additionally, there are some specific diagnostic tests that may help better define the lesion localization (e.g. CK serum levels, electrophysiology and an edrophonium test) (see below).

DIFFERENTIAL DIAGNOSIS FOR NEUROMUSCULAR WEAKNESS AND COLLAPSE

The differential diagnoses to be considered depend on the lesion localization in addition to the signalment, history and response to previous treatment attempts. For this reason, the potential NM causes of acute generalized weakness and collapse need to be considered separately by dividing them into:

- Neuropathies.
- Junctionopathies (NM transmission diseases).
- Myopathies.

Specific diagnostic tests

The tests listed below and in *Table 48* (p. 186) should be considered in any case of acute exercise-associated weakness or collapse, although the diagnostic plan needs to be specifically addressed after taking into consideration the suspected underlying cause (**142**).

Rule-out systemic aetiologies

- **Routine blood tests and urine analysis.** Haematology, complete serum biochemistry and urine analysis should all be considered as the minimum essential database, together with chest radiography and abdominal ultrasound.
- **Serum CK levels.** Evaluation of serum CK concentration should be a part of the NM minimum database and may be indicative of active muscle disease in canine and feline patients. The serum half-life of CK is very short, lasting only 6 hours; a persistent elevation of 4–5 times the normal level in two tests carried out between 24 and 48 hours of each other is an indication of a recent and active muscle lesion. CK may be normal in the presence of muscle disease, therefore muscle disease should not be ruled out based on a normal CK concentration. Serum CK may also be mildly elevated in the absence of NM disease related to factors such as exercise, recumbency, trauma such as intramuscular injections, or markedly elevated in anorexic cats. Elevations of CK are most dramatic in the muscular dystrophies or with myonecrosis (× 100 normal), moderately elevated in inflammatory myopathies (× 10 normal) or normal or only mildly elevated in other diseases such as myotonia congenita.

▶ **142 Diagnostic approach to exercise-associated weakness.**

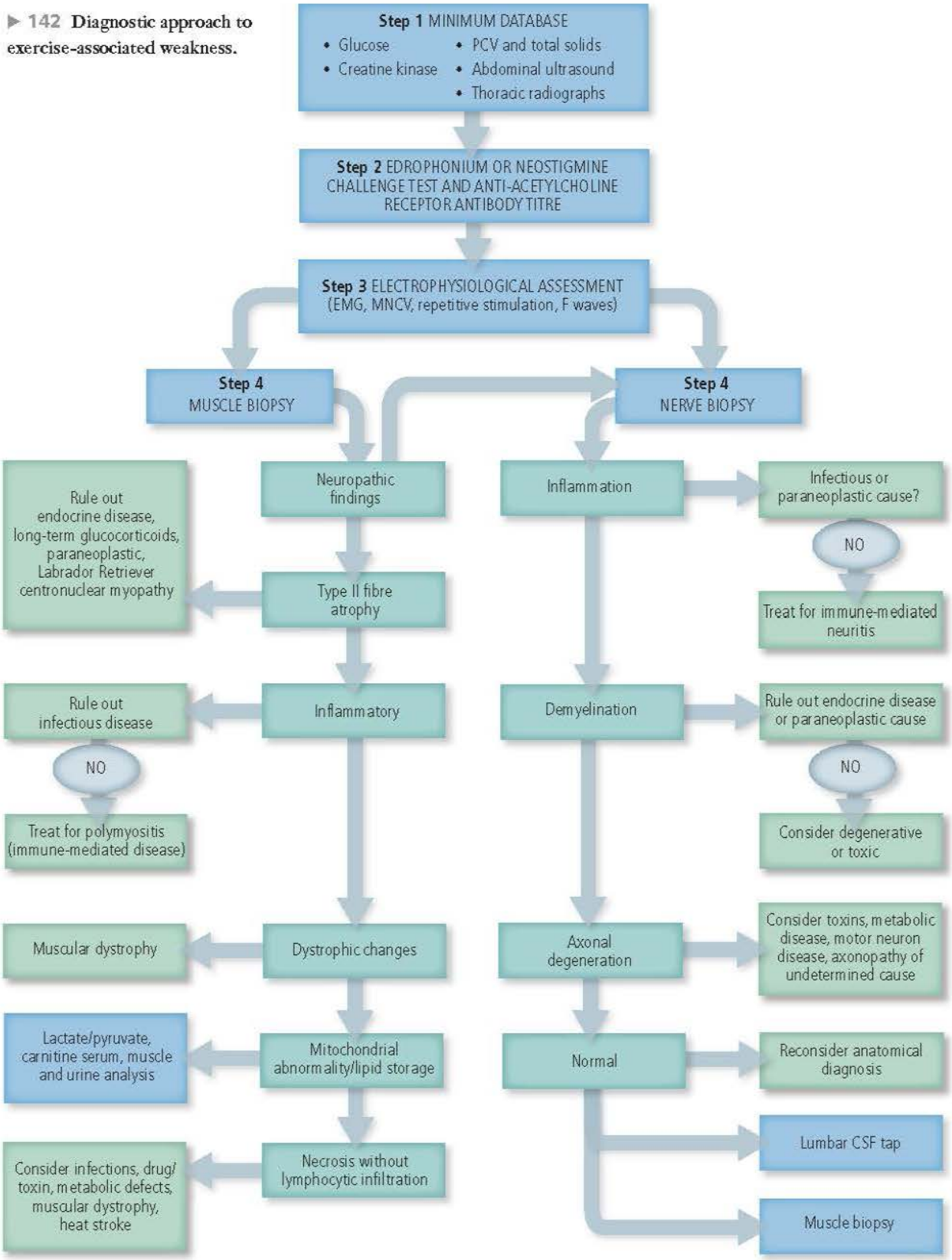


Table 48 **Specific laboratory tests and associated diseases**

LABORATORY TEST	ABNORMALITY	SUSPECTED DISEASE
Thyroid hormone testing	Decreased fT4, tT4 and increased TSH (D)	Hypothyroidism (hypothyroid neuropathy/myopathy)
Serum glucose and serum insulin level	Hypoglycaemia Inappropriately increased insulin levels	Hypoglycaemia-associated neuropathy Insulinoma
Cerebrospinal fluid	Albumino-cytological dissociation (increased protein associated with normal TNCC)	Nerve root disorders (polyradiculoneuritis)
Serum *Neospora caninum* and *Toxoplasma gondii* titres or PCR	Elevated titres or positive PCR	*Neospora* and *Toxoplasma* infection
Plasma cholinesterase	Decreased plasma levels	Organophosphate toxicity
Serum glucose level or fructosamine and glycosylated haemoglobin levels	Persistent hyperglycaemia	Diabetes mellitus (diabetic neuropathy)
Plasma lactate and pyruvate	Elevated concentrations of resting and post-exercise lactate and lactate: pyruvate ratios	Metabolic, mitochondrial myopathies
Plasma, urine and muscle carnitine concentration	Reduced plasma and muscle carnitine, increased urine excretion of carnitine esters	Metabolic, mitochondrial, lipid storage myopathies
Serum anti-AChR antibody	Antibody titre >0.6 nmol/l (D) Antibody titre >0.3 nmol/l (C)	Acquired myasthenia gravis
Serum CK	Severely elevated CK (x100 normal) Moderately elevated CK (x10 normal)	Muscular dystrophies or myonecrosis Inflammatory myopathies

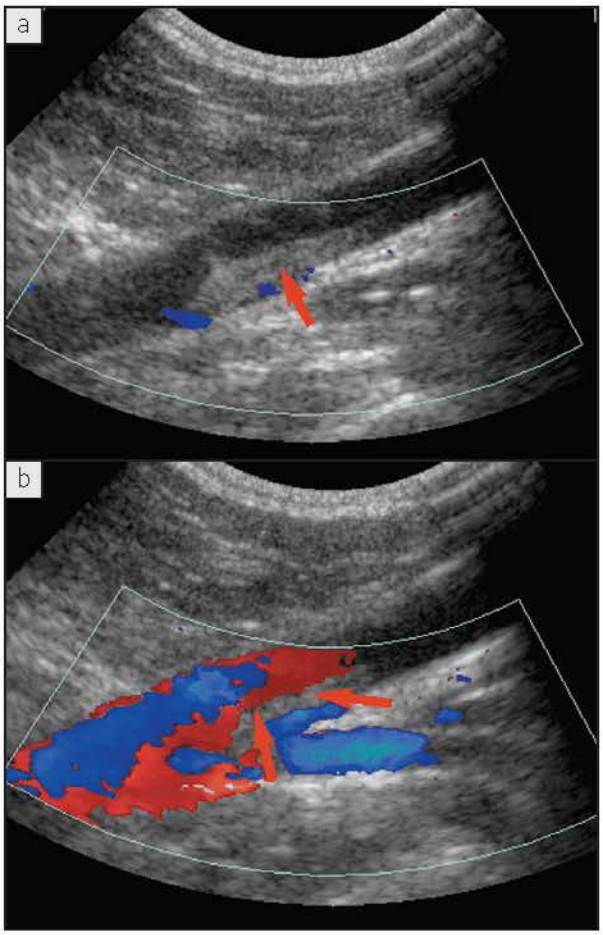
D = dog; C = cat.

Modified from Glass EN, Kent M (2002) The clinical examination for neuromuscular disease. *Vet Clin North Am Small Anim Pract* **32**:1–29.

- **Radiography and ultrasound.** May reveal primary cause of NM dysfunction, such as other major organ diseases, neoplasia and major blood vessel abnormalities, and the consequences of NM diseases, including megaoesophagus or aspiration pneumonia (**143, 144**).
- **Thyroid function testing (total T4, free T4, TSH) and ACTH stimulation test.** These tests should always be considered, as NM disease may be the only sign of endocrine diseases.
- **Serology/PCR for infectious agents or autoimmune conditions.** Serology for autoimmune conditions, such as systemic lupus erythematosus and acquired MG, may be considered; antibodies against the AChR need to be measured in all cases of exercise-induced weakness, especially if megaoesophagus is present.

Neuromuscular system function

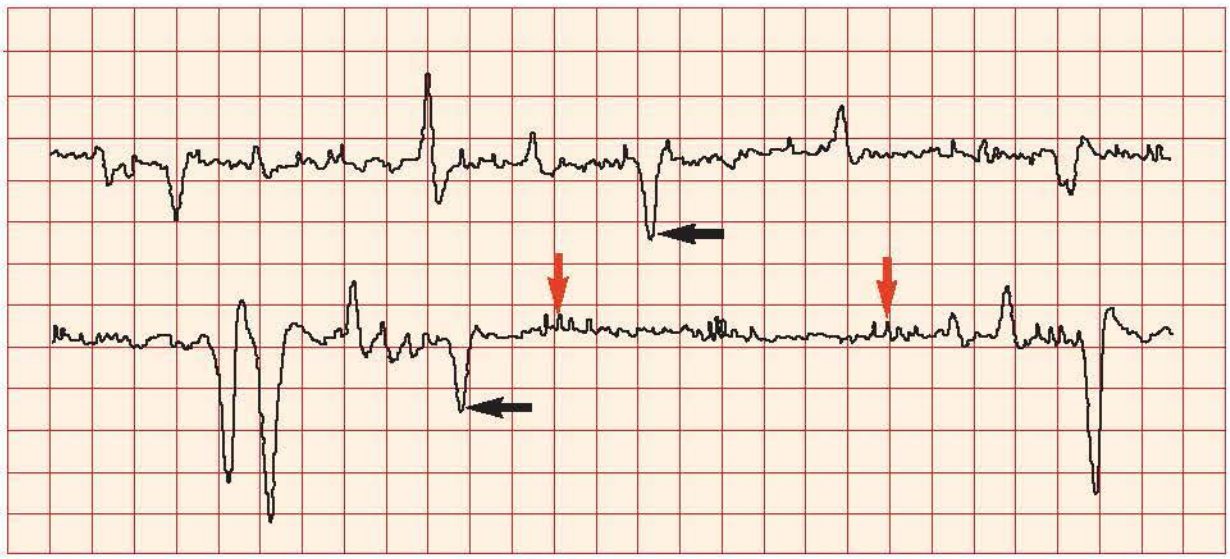
- **Electrophysiology.** Although diagnosis of a specific NM condition is rarely obtained by electrophysiological testing, it can be essential to classify the NM condition as a junctional, axonal, myelin or myopathic disorder and to define the distribution and severity of the disease in order to better define the differential diagnosis (**145**).



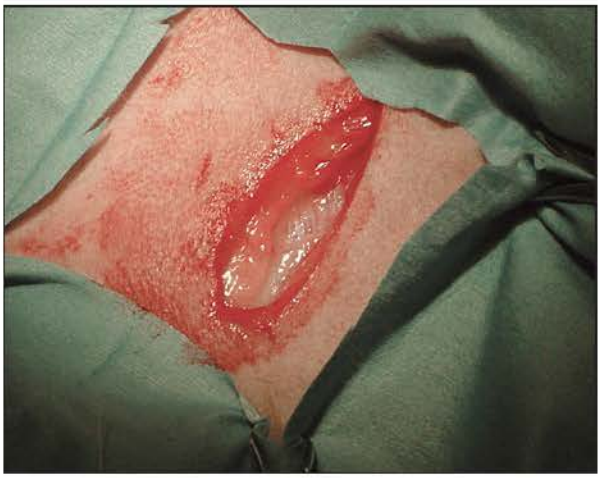
◀ 143 (a) Doppler ultrasonography of the femoral artery reveals an intraluminal mass compatible with a thrombus (arrow). (b) Doppler ultrasonography confirms the altered blood flow around this lesion (arrows).

▼ 144 Lateral radiograph demonstrating mega-oesophagus. The arrows mark the dorsal and ventral boundaries of the caudal thoracic oesophagus.





▲ 145 Needle electromyography can reveal the presence of positive sharp waves (black arrows) and fibrillations (red arrows), which are compatible with axonal or muscle disease and tend to rule out neuromuscular junction diseases.



▲ 146 A muscle biopsy should be performed in a routine sterile manner. Once a linear incision has been made in the skin overlying the muscle of choice, the subcutaneous fat is dissected to reveal the shiny muscle fascia.

- **Muscle and nerve biopsy.** Necessary to provide a specific diagnosis; requires interpretation in conjunction with clinical signs and results of other tests including electrophysiology (**146**).

Specific tests

Many of the tests outlined below are only performed at selected laboratories. The clinician is advised to contact the laboratory prior to acquiring and submitting the samples for details.

- **Evaluation of lactate and pyruvate levels.** Lactic acid is the product of anaerobic metabolism of glucose, therefore it may be increased in normal animals after anaerobic exercise. Lactic acidosis, however, can result from a defect in anaerobic metabolism, secondary to pyruvate deficiency. Plasma lactate (L) and pyruvate (P) and their L:P ratio in blood are evaluated in metabolic myopathies and are essential for the diagnosis of mitochondrial diseases characterized by high serum lactate and pyruvate concentrations with a high L:P ratio compared to normal.
- **Quantitative urinary organic acid analysis.** Organic aciduria can be due to inborn metabolic errors causing accumulation of non-metabolizable organic acids in tissues such as muscle and brain. Their excess can be detected in urine. Organic aciduria can result in intermittent weakness and collapse.
- **Carnitine evaluation in blood, muscle and urine.** Primary or secondary carnitine metabolism disorders are diagnosed by a complete evaluation of the carnitine status in the body. This is done by measurement of carnitine in urine, blood and muscle in its three different forms: total, free and esterified.
- **Cerebrospinal fluid analysis.** Rarely useful in the evaluation of a primary NM condition; a lumbar CSF tap may be performed if a diffuse inflammatory condition affecting the nerve roots (polyradiculoneuritis) is suspected. Specific PCR for infectious agents may be performed on CSF if a diffuse inflammatory condition is suspected.

COMMON NEUROMUSCULAR CAUSES OF EXERCISE-INDUCED WEAKNESS AND COLLAPSE

Myasthenia gravis is described in detail elsewhere in this book (Chapter 24).

Exercise-induced collapse

Overview

Young (7 months–2 years old) Labrador Retrievers of either sex have been reported with acute weakness and collapse during heavy training. The condition has also been described in Chesapeake Bay Retrievers, Curly-coated Retrievers, Border Collies and Welsh Pembroke Corgis.

Clinical presentation

Affected animals are normal at rest and have normal levels of physical activity. Acute and progressive generalized weakness, ataxia and eventually collapse during exercise activity of variable duration (5–15 minutes) are most commonly seen in affected animals. Animals affected often show severe hyperthermia (>41.5°C [106.7°F]) during episodes, although comparable severe hyperthermia is also recorded in normal exercising Labrador Retrievers. Affected animals usually fully recover after 10–20 minutes of rest, but the condition can be fatal.

Recently a mutation of the Dynamin 1 gene (*DNM1*), responsible for a molecule essential in synaptic vescicle endocytosis, has been associated with the syndrome of exercise-induced collapse. This mutation has been observed in Labrador Retrievers, Chesapeake Bay Retrievers, Curly-coated Retrievers and Welsh Pembroke Corgis. Clinical signs are observed in the homozygous state; 30–40% of pure Labrador Retrievers have been noted as carriers of the mutation, without any clinical importance.

Diagnosis

Diagnosis is exclusional and based on clinical findings, as laboratory, electrophysiological and histopathological tests are normal. Severe alkalosis during the event may be the only laboratory finding. Genetic testing has recently become available at the Veterinary Diagnostic Laboratory, University of Minnesota.

Management

No specific treatments have as yet been proven beneficial. Exercise restriction is necessary to avoid relapse. The prognosis is good when providing exercise restriction.

Idiopathic immune-mediated inflammatory myopathy (polymyositis)

Overview

The condition affects dogs and rarely cats. No breed, sex or age predispositions exist, although breed-specific variants are reported in Newfoundlands, Boxers and Vizslas. This generalized inflammatory myopathy is not associated with any infectious disease and is histologically characterized by a predominantly lymphocytic infiltration within skeletal myofibres (**147**). Sarcolemma-specific autoantibodies have been identified in a population of dogs with polymyositis, particularly in the Boxer and Newfoundland breeds. Cancer may be associated with canine and feline inflammatory myopathies (lymphoma, anaplastic round cell tumour or plasmacytoma).

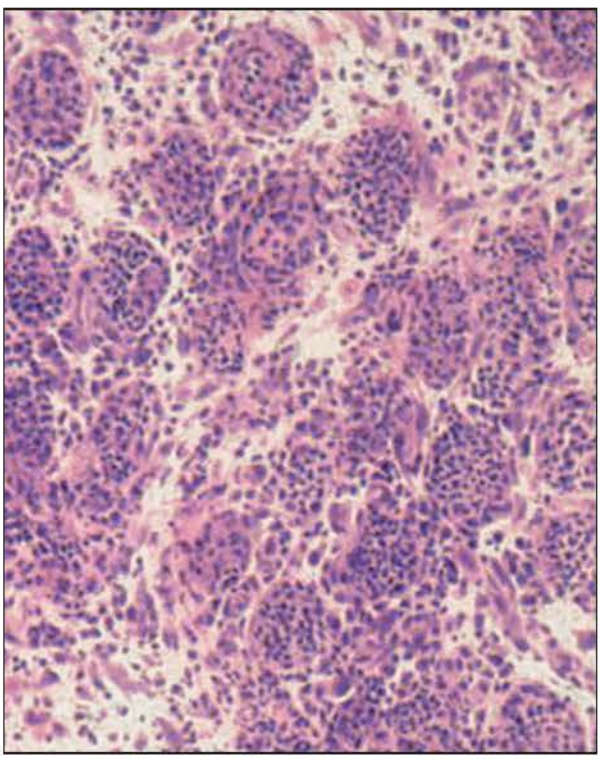
Skeletal muscles are usually diffusely affected, although focal forms involving pharyngeal, laryngeal or oesophageal muscles have been described. Other organs and systems may be involved in canine polymyositis, including the heart (myocarditis), gastrointestinal tract (inflammatory bowel disease), thyroid (thyroiditis) and skin.

Clinical presentation

Progressive intolerance to exercise, with acute and generalized weakness, is the most common presentation. Marked weight loss is relatively common, while myalgia is not a consistent finding.

Diagnosis

Diagnosis is based on specific clinical signs, marked elevation of CK concentration, compatible electrophysiological findings, histopathology and negative infectious agent titres (*Toxoplasma gondii*, *Neospora caninum* and tick-related disease when appropriate in dogs; *T. gondii*, feline leukaemia virus and feline immunodeficiency virus in cats).



▲ **147** **Histopathology confirming a marked mononuclear cell infiltration of the muscle compatible with polymyositis. (H&E)**



▲ 148 **Physiotherapy, including the use of electrical muscle stimulators, is vital for promoting the best possible recovery.**

Management

Therapy with prednisolone at immunosuppressive dosages (2 mg/kg PO q12h in dogs; 3 mg/kg PO q12h in cats), with tapering of the dose every 2–4 weeks, may result in clinical resolution. Addition of oral azathioprine (2 mg/kg q24h until remission, then 0.5–2 mg/kg q48h) can be considered if there is failure to respond with prednisolone only or in cases of relapse.

All cases that clinically relapse should have repeat muscle biopsy, as some cases demonstrate neoplastic progression. Serum CK concentration is a good marker of treatment response and should be monitored during therapy.

Opioid analgesia should be considered in the first days in the few cases that exhibit severe muscle pain. Supportive care, including nutritional management and physiotherapy (**148**), is essential to control muscle wastage in non-ambulatory dogs. Oesophageal or gastrostomy tubes may be necessary to support nutritional management.

The prognosis with early and aggressive initial treatment may be good unless concurrent megaoesophagus or pharyngeal paralysis is observed. Early diagnosis and treatment limit the severe myofibre loss and fibrosis associated with a poor prognosis. Relapse is possible and is associated with a poor prognosis.

Infectious/inflammatory myopathies/polyneuritis

Overview

Protozoal (*Toxoplasma gondii*, *Neospora caninum*, *Leishmania infantum*, *Hepatozoon canis*), rickettsial (*Ehrlichia canis*) and, less commonly, bacterial (*Clostridium* spp., *Leptospira icterohaemorrhagiae*) infections may cause acute and generalized weakness in patients as part of a multisystemic infection. No specific breed is overrepresented. Immunocompromised animals, including young patients or older dogs with concurrent disorders, are predisposed.

Diagnosis

Diagnosis depends on identification of the infectious agent in muscle tissue with molecular or immunohistochemical methods. Elevation of CK concentration and an electromyogram (EMG) examination are not specific. Positive serological titres sometimes cannot differentiate between an exposed versus an infected animal, as a mild/moderate positive titre can be seen in animals previously exposed to the organism, while false negatives are observed in acute stages or in severely immunocompromised patients.

Management

Protracted treatment with specific antibiotics or antimonials is often required: trimethoprim-sulphadiazine (15 mg/kg PO q12h for 4 weeks); clindamycin (15 mg/kg PO q12h for 4 weeks); pyrimethamine (1 mg/kg PO q24h for 2 weeks in dogs).

The prognosis is guarded, depending on clinical stage and time of diagnosis. If treatment has been initiated early, loss of function may be partial; physiotherapy is mandatory to reduce muscle atrophy.

(Exertional) rhabdomyolysis

Overview

Rhabdomyolyis is a clinical syndrome characterized by acute muscle necrosis with muscular pain, weakness/collapse, marked increases in CK levels and myoglobinuria. Common causes include excessive exertion, as described in racing dogs, trauma, severe hyperthermia (heat stroke), toxins and drugs, and salt and water imbalances resulting in severe electrolyte imbalance and infectious diseases. In some cases the primary cause may be difficult to diagnose.

Clinical presentation
Direct sarcolemmal injury or failure of muscular energy supply leads to increased intracellular calcium levels, with secondary necrosis of myofibres. Severe myoglobin release from myofibre injury may cause acute renal tubular necrosis with acute renal failure. Myocardial and respiratory failure have been recently reported due to cardiac and intercostal/diaphragmatic myonecrosis.

Diagnosis
Muscle biopsy is mandatory for a diagnosis. Histology is characterized by a necrotizing myositis.

Management
Therapy aims to control electrolyte imbalance, support muscular oxidative metabolism with L-carnitine (50 mg/kg PO q12h), increase activity of mitochondrial enzymes through coenzyme Q_{10} administration (100 mg PO q24h) and decrease lipid storage in muscle by administration of riboflavin (100 mg PO q24h). Treatment should aim at maintaining good urinary output through fluid therapy and diuretics (mannitol or/and furosemide). Muscle relaxation can be achieved by targeting the calcium movement at the sarcoplasmic reticulum with dantrolene administration (1.5 mg/kg IV q8h). Muscle pain should be controlled with either fentanyl or gabapentin administration.

The prognosis is guarded. With early and appropriate supportive therapy, acute rhabdomyolysis can be a reversible disorder.



▲ 149 Cervical ventroflexion in a cat.

Hypokalaemic myopathy
Overview
Hypokalaemic myopathy is observed in cats and, very rarely, in dogs. It results from reduced potassium intake, increased potassium loss (chronic renal failure) and congenital predispositions (Burmese cat). Hypokalaemia affects myofibres, which become progressively refractory to depolarization. The muscle cell membrane increases its permeability to sodium ions, causing hypopolarization and acute weakness or collapse.

Clinical presentation
Generalized weakness with ventroflexion of the neck is often seen (**149**). In severe stages, weakness may progress to acute collapse.

Diagnosis
Diagnosis is reached by measurement of serum potassium levels (≤3.5 mmol/l [3.5 mEq/l]). Chronic renal failure with potassium loss in the urine and hyperthyroidism should be immediately ruled out. CK levels may be increased due to muscle fibre necrosis, which is visible on muscle biopsy.

Management
Supplementation with potassium gluconate (2–4 mmol [mEq] q12h) orally can be used; however, in severe weakness, intravenous potassium chloride supplementation (0.2–0.4 mmol [mEq]/kg/hour) is required with cardiac monitoring.

In general, the prognosis is good if potassium levels are supplemented and the primary cause of the hypokalaemia is treated.

Mitochondrial myopathy

Overview

Mitochondrial myopathy is a rare metabolic myopathy reported in various canine breeds. Mitochondrial myopathies are a group of disorders characterized by abnormalities of mitochondrial enzyme function. These cause a defect in the anaerobic metabolism of pyruvate in the muscle, leading to severe lactic acidaemia.

Clinical presentation

Combinations of brain and muscular signs, in particular exercise intolerance and weakness, are often observed.

Diagnosis

Diagnosis can be challenging and is based on:

- Documentation of high serum lactate and pyruvate concentrations, with high L:P ratios pre- and post-exercise and pre- and post-food intake.
- Muscle biopsy is characterized by massive proliferations of mitochondria in myofibres, called 'ragged-red' fibres due to their red staining with the Gömöri modified trichrome stain.
- Definitive diagnosis is obtained by biochemical and molecular testing, and is difficult to perform.

Management

No specific treatments are currently available. Supportive care and treatment to support muscular oxidative metabolism, such as L-carnitine (50 mg/kg PO q12h) and coenzyme Q_{10} (100 mg PO q24h) may temporarily improve muscular strength.

ATAXIA

Jonathan Levine

INTRODUCTION

Ataxia is defined as incoordination that results from either insufficient proprioceptive (sensory) input to gait centres in the CNS or failure of the central regulators of motor function, such as the cerebellum. Paresis (weakness) due to UMN or LMN lesions often accompanies ataxia and in many cases contributes to the observed gait deficits. Animals with ataxia may exhibit crossing of the limbs, falling, leaning and overreaching, as well as disorganized range and rates of movement, as single signs or in combinations.

Limb movement associated with ataxia can be described as follows:

- **Dysmetria.** An aspect of ataxia in which the ability to control the distance, power and speed of an action is impaired. Usually used to describe abnormalities or movement associated with cerebellar disorders.
- **Hypermetria.** Ataxia characterized by overreaching a desired object or goal. Usually seen with cerebellar disorders.
- **Hypometria.** Ataxia characterized by underreaching an object or goal. Usually seen with cerebellar disease. A similar gait is seen more often with LMN paresis.

In veterinary medicine, ataxia is typically classified as GP, vestibular or cerebellar in origin. Although some animals may exhibit ataxia that reflects a combination of these subclasses, accurate lesion localization is essential in establishing an appropriate list of differential diagnoses and a diagnostic plan.

NEUROANATOMICAL BASIS

The processes involved in gait initiation, generation and coordination are still poorly understood in veterinary species. Gait is believed to be initiated in midbrain nuclei, which signal, through UMN projections, to local gait-generating neurons within the spinal cord. Sensory system input is essential in coordinating these motor responses. GP receptors are located within joints, muscles and tendons. Changes in body position result in receptor discharge and the stimulation of primary afferent (sensory) neurons. These primary neurons project to the spinal cord, where signals ascend through the dorsal columns and lateral funiculi to brainstem structures. Vestibular (special proprioceptive) receptors located in the inner ear are also essential in gait coordination. Fibres associated with these receptors interact with the vestibular nuclei in the brainstem to help maintain the position of the eyes, neck, trunk and limbs with respect to the position and movement of the head.

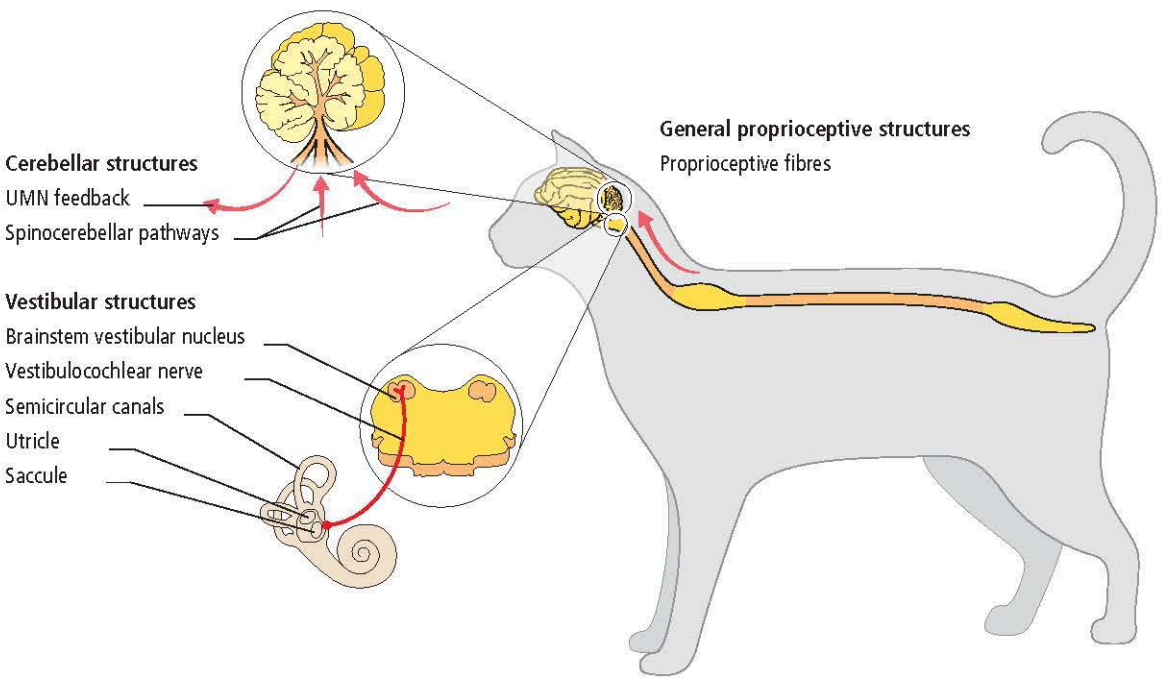
In addition to appropriate proprioceptive input, gait coordination relies on interaction between the cerebellum and motor systems. The cerebellum controls the rate, range and force of movements, without actually initiating motor activity. It receives sensory input from proprioceptive, visual and auditory systems. UMNs also project to the cerebellum and the cerebellum provides feedback information to UMNs in the brainstem and cerebral cortex via deep cerebellar nuclei. Because of its close association with the brainstem vestibular nuclei (see Chapter 14), the cerebellum also functions in the maintenance of equilibrium. Ultimately, the complex interaction between the cerebellum, motor systems and

sensory systems serves to 'smooth' voluntary movements induced by the UMNs, regulate muscle tone and preserve equilibrium (**150**).

General proprioceptive ataxia

GP ataxia is probably the most common form of ataxia recognized in domestic species. It results from lesions affecting the primary afferent neuron or the ascending proprioceptive tracts within the spinal cord and brainstem (midbrain, pons, medulla). Therefore, animals with GP ataxia may have additional neurological signs reflecting a spinal cord or brainstem localization. Although lesions within the thalamus and cerebral cortex will cause GP ataxia in humans, in domestic species the ataxia generated from lesions within these structures is usually too subtle to be detected on gait evaluation. The pathways of the GP sensory system are anatomically adjacent to most of the UMN pathways necessary for gait generation. The change in the gait therefore generally reflects a combined dysfunction of both UMN paresis and GP ataxia, with delayed onset of protraction of the limb and lengthened stride. From a lesion localization point of view, UMN paresis and GP ataxia visible in the gait can occur as a consequence of a lesion affecting the brainstem or spinal cord.

Compared with UMN paresis, disorders of the LMNs usually cause paresis and not ataxia. The degree of paresis varies from a short stride to a complete inability to support weight, causing collapse of the limb whenever weight is placed on it. Although most peripheral neuropathies are likely to affect both motor and sensory axons, gait dysfunction principally reflects LMN paresis. The exception is with the so-called sensory neuropathies, which initially can present primarily with ataxia.



▲ **150** **Schematic drawing illustrating structures that can be affected in animals with ataxia. General proprioceptive ataxia is most frequently seen with spinal cord lesions, due to disruption of ascending projections in the dorsal and lateral funiculi. It is also recognized in some animals with caudal brainstem and peripheral nervous system diseases. Vestibular ataxia may result from lesions within the inner ear or vestibular nuclei, which are located in the medulla oblongata. Head tilt, leaning, falling and a broad-based gait are characteristic. The cerebellum receives proprioceptive and upper motor neuron projections. It serves to smooth movements via modulating upper motor neuron tone. Lesions within the cerebellum can lead to ataxia, characterized by dysmetria and hypermetria.**



▲ **151** Serial photographic images of a cat with severe cerebellar and vestibular ataxia. Note the presence of falling and head tilt to the right (b) and as the cat attempts to stand, the ataxia results in a roll to the side. Complete body rolls can be seen with vestibular ataxia.

Vestibular ataxia

Vestibular ataxia occurs with lesions affecting either the peripheral or central vestibular apparatus. In addition to ataxia, animals will often have concurrent neurological signs that reflect a vestibular disorder (e.g. head tilt or head sway, pathological nystagmus or positional strabismus). Animals with vestibular ataxia often have a broad-based gait (especially in the hindlimbs), with leaning towards the side of decreased vestibular tone. Some animals may have substantial swaying when walking and will occasionally fall; recumbent animals may be seen to roll (**151**). Weakness or paresis is only seen with central vestibular disease and is not a feature of peripheral vestibular disease.

Cerebellar ataxia

Cerebellar ataxia can be seen in animals that have lesions within the cerebellar cortex. Other signs of cerebellar disease, such as intention tremors, are often present. Cerebellar ataxia is characterized by hypermetria and dysmetria. Hypermetria associated with cerebellar ataxia consists of overflexion during limb protraction and is therefore distinct from the overreaching, long-strided gait noted in animals with combined GP ataxia/UMN paresis. Dysmetria is a component of cerebellar ataxia and is manifest by a loss of synchronous limb movements.

NEUROLOGICAL EVALUATION

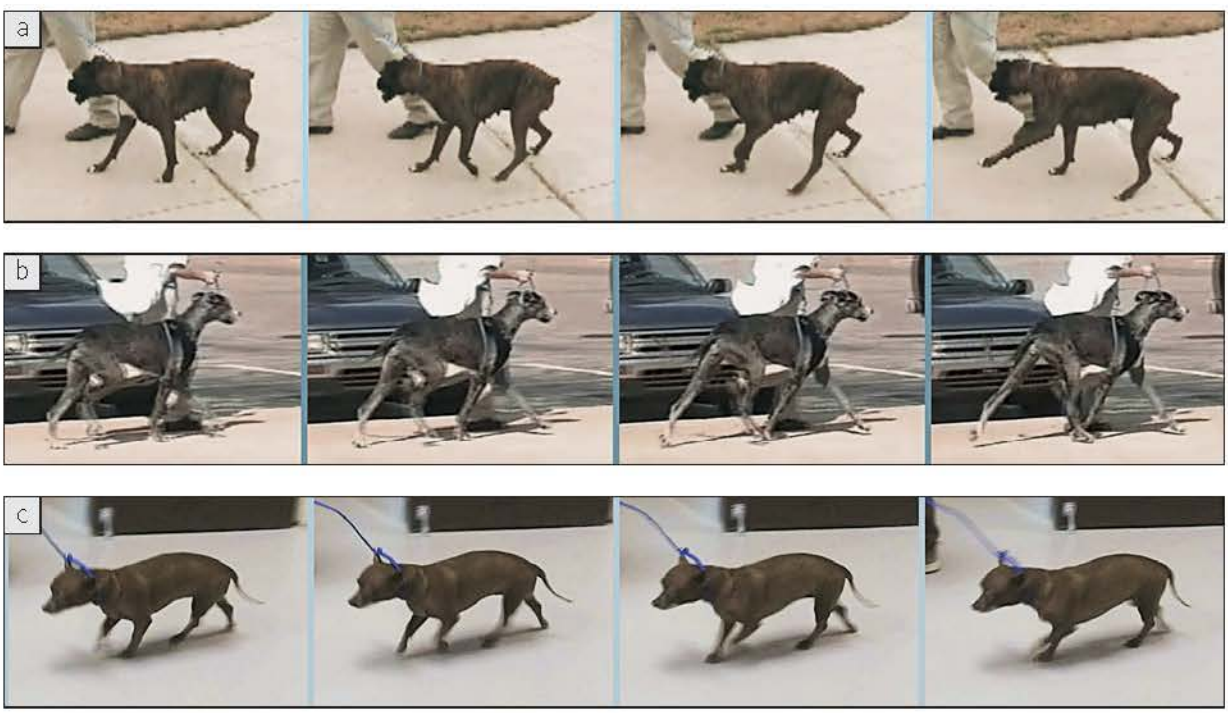
At the outset of the neurological evaluation, the examiner must first determine whether the gait abnormalities seen are truly indicative of ataxia (**152**). Lameness, various orthopaedic gait disturbances and weakness due to non-neurological disease must be excluded (see Chapter 16).

▼ **152** Various forms of neurological gait disturbance. (a) Dog with a left cerebellar ischaemic territorial infarct. Hypermetria is seen best in the left forelimb. Note the preservation of carpal flexion in frames 2 and 3, with sudden overreaching seen in frame 4. Dysmetria can also be appreciated as a lack of synchrony between limbs. (b) Dog with C4/C5 spinal cord compression due to spondylomyelopathy. Note the long-strided gait in all four limbs, with a relative lack of flexion at the carpal and hock joints. These findings suggest upper motor neuron paresis and general proprioceptive ataxia affecting all the limbs. (c) Dog with C6/C7 spinal cord compression due to disc extrusion. The forelimb gait is markedly short strided, indicating lower motor neuron paresis associated with C6–T2 spinal cord segment involvement.

Step 1. Is the animal ataxic?

Lameness is defined as a reluctance to bear weight on a limb, and is often the result of orthopaedic conditions or, less commonly, diseases affecting afferent (sensory) neurons. Lameness, unlike ataxia, may be episodic and should not be characterized by dragging, scuffing or crossing over of the limbs. However, lameness and ataxia can exist concurrently, especially in older dogs that have neurological and orthopaedic disease.

Other gait disturbances are possible with orthopaedic disease in addition to lameness, especially short striding. This can occur in animals with hip dysplasia, elbow arthritis or polyarthritis (typically all limbs) and is related to joint pain. Again, crossing over of the limbs, dragging and knuckling should not be present. Orthopaedic disease can interfere with certain elements of the neurological examination. For example, the hopping assessment may be falsely diminished in animals that have joint or bone pain. Joint pain may also result in false reduction of flexor withdrawal reflexes.



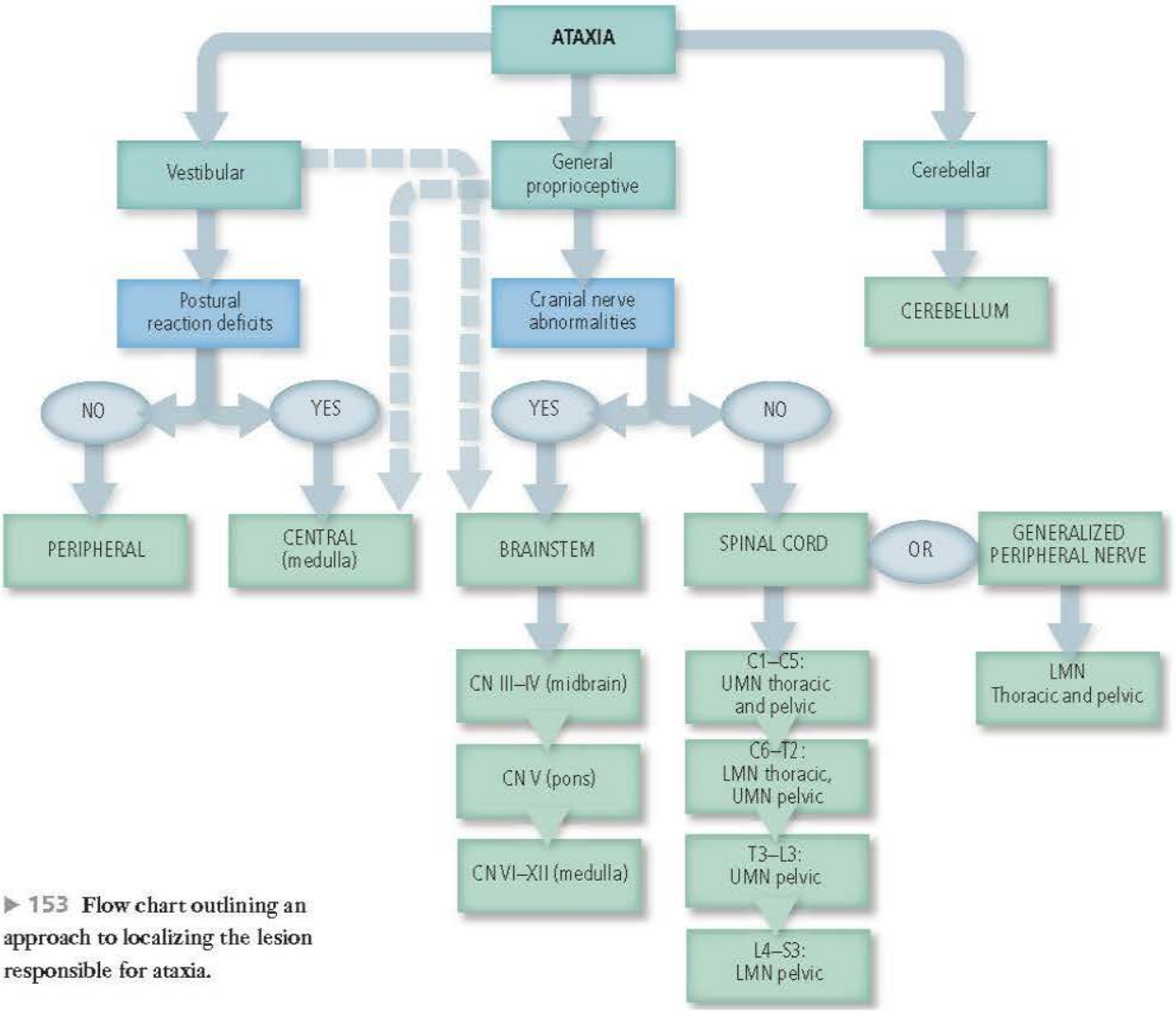
Finally, systemic illnesses (e.g. cardiac disease) and metabolic derangements can appear to cause gait dysfunction similar to that seen with structural neurological disease. For example, cardiac failure can lead to hypoperfusion and hypoxia, both of which may result in poor oxygen delivery to CNS structures. Addison's disease can induce profound weakness due to low circulating cortisol levels, hyperkalaemia and hypovolaemic shock. Typically, weakness resulting from systemic illness will not lead to ataxia. However, some systemic illness can cause structural nervous system lesions. For example, animals with sepsis may develop ischaemic infarction within the CNS secondary to hypercoagulability and the release of inflammatory mediators. The interrelationship between systemic illness and the nervous system underscores the necessity to correlate neurological examination findings with a standard physical examination and screening ancillary diagnostics.

Step 2. Is the ataxia cerebellar, vestibular or general proprioceptive in origin?

If ataxia is present, the next step is to determine the portion of the nervous system that is affected and contributing to the observed gait disturbance (**153**, *Table 49*). In this regard it is often useful to try and characterize which classification(s) of ataxia is/are contributing to the gait pattern. The presence of ataxia should suggest a lesion of the spinal cord, brainstem, cerebellum or vestibular system as discussed above. Multifocal disease with involvement of at least two of these regions should also be a consideration. Correct anatomical diagnosis is crucial in establishing a differential list, as some causes of ataxia are specific to certain regions of the nervous system. Additionally, the choice of ancillary diagnostic tests is guided by lesion localization and the differential list. *Table 49* and the flowchart **153** (next page) are provided as a quick reference to correlate gait and neurological examination characteristics with lesion location.

Table 49 **Types of ataxia and associated localizing signs**

TYPE OF ATAXIA	ANATOMICAL DIAGNOSIS	NEUROLOGICAL SIGNS
Proprioceptive	General proprioceptive pathways: • Spinal cord • Brainstem	Abnormal postural reactions. Concurrent UMN paresis in limbs and normal to increased spinal reflexes. No effect on the eyes or head posture
Vestibular	Vestibular apparatus: • Vestibular nuclei (central) • Vestibular portion of CN VIII or vestibular receptors (peripheral)	**Unilateral lesion.** Head tilt, leaning, falling or rolling to one side, abnormal nystagmus, strabismus, normal (peripheral) or abnormal (central) postural reactions **Bilateral lesion.** Crouched posture, reluctance to move and wide head excursion
Cerebellar	Cerebellum	**Diffuse lesion.** Broad-based stance, symmetrical ataxia, hypermetria, truncal ataxia, intention tremor of the head, vestibular deficits, delayed and then exaggerated response to postural reaction testing, menace deficit with normal vision, no paresis and normal mentation **Unilateral lesion.** Ipsilateral deficits except for vestibular deficits, which are contralateral



▶ **153** **Flow chart outlining an approach to localizing the lesion responsible for ataxia.**

DIFFERENTIAL DIAGNOSIS

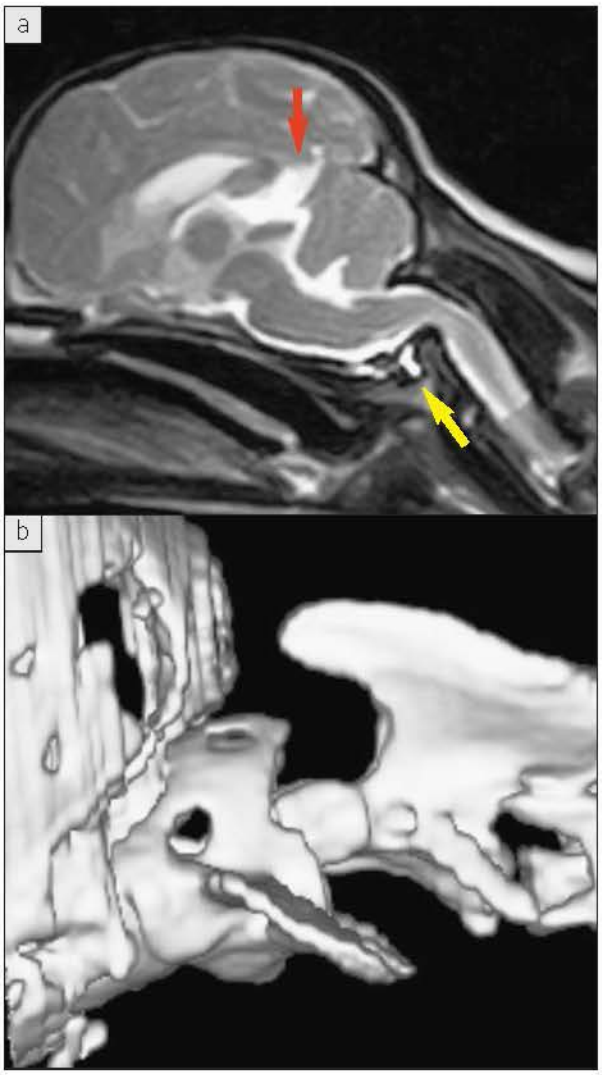
A differential diagnosis list should be established based on the neuroanatomical origin of the ataxia. *Table 50* (p. 201) outlines common causes of ataxia, listed by lesion localization (spinal cord, caudal brainstem, cerebellum and vestibular system). Diseases that affect the alpha motor neuron, NM junction and muscle will result in paresis without ataxia and therefore have not been included (for further information, see Chapter 10). Differentiating ataxia from paresis based on gait and postural testing can be challenging; therefore, the clinician must be willing to consider including all possibilities when generating differential lists if the animal does not have a gait that is easy to define.

Specific diagnostic tests

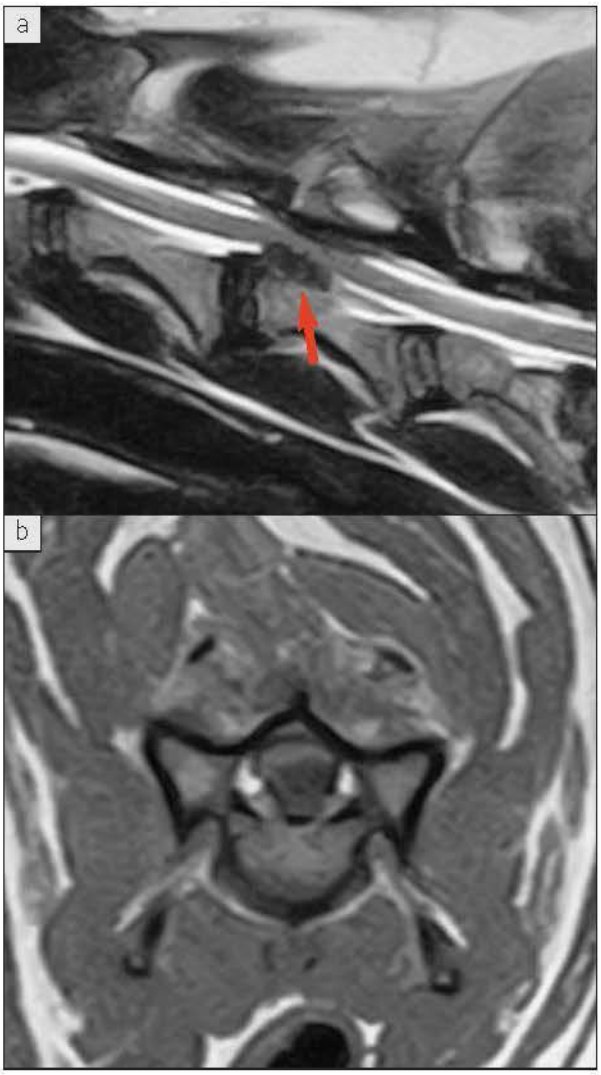
Appropriate diagnostic test selection is dependent on the region of the nervous system affected.

Spinal cord disease (**154, 155**)

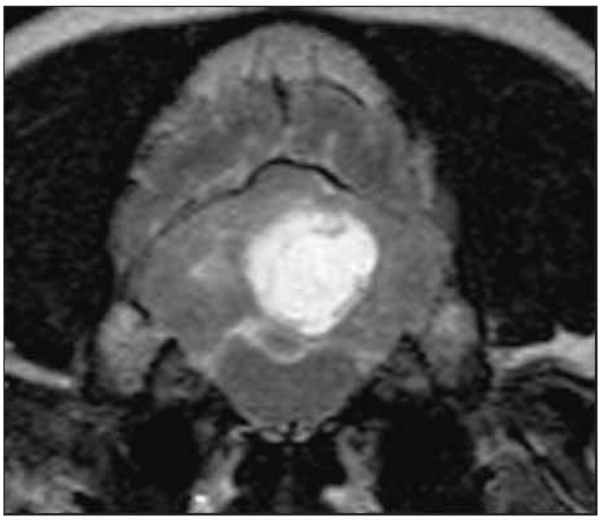
- CBC and serum biochemistry.
- Screening thoracic and abdominal radiography and ultrasonography to rule out metastatic diseases.
- Vertebral column radiographs as a cost-effective screening test to identify obvious vertebral fractures, luxation, osseous lytic tumours and discospondylitis.
- Advanced imaging, preferably MRI rather than CT.
- CSF analysis.



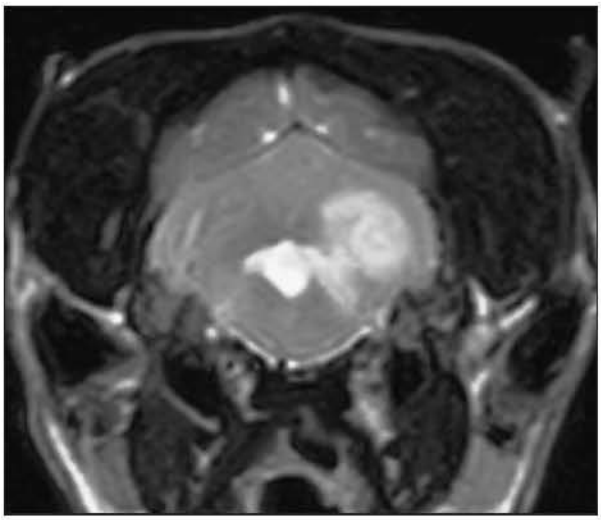
▲ 154 Sagittal T2-weighted MR image (a) and 3-dimensional bone-windowed CT reconstruction (b) of a dog with proprioceptive ataxia in all limbs. The MR image shows severe atlantoaxial subluxation as evidenced by dorsal displacement of C2 and widening of the C1/C2 articulation (yellow arrow). The spinal cord is severely compressed by the displaced dens and is focally hyperintense. There is also a moderate-sized quadrigeminal cyst (red arrow) resulting in compression of the rostral cerebellum, tenting of the 4th ventricle and subtle compression of the caudal cerebellum due to Chiari-like malformation (these findings are probably incidental). The CT image shows a defect in the occipital bone and dorsal displacement of C2.



▲ 155 T2-weighted sagittal (a) and T1-weighted transverse (b; at the C3/C4 articulation) MR images from a 5-year-old Cocker Spaniel with ambulatory tetraparesis and general proprioceptive ataxia in all limbs. There is marked ventral extradural spinal cord compression due to hypointense extruded disc material (arrow, a) that predominantly overlies the body of C4.



▲ 156 Transverse T2-weighed MR image from a 4-year-old Cairn Terrier with cerebellar and vestibular ataxia. Within the right cerebellum, caudal cerebellar peduncle and medulla there is a poorly marginated hyperintense lesion. Further diagnostics suggested granulomatous meningoencephalitis as the likely aetiology.



▲ 157 Transverse T2-weighed MR image from a 6-year-old Cocker Spaniel with progressive cerebellar ataxia. There is a well marginated, round, high signal lesion within the cerebellum. Biopsy identified the lesion as an anaplastic astrocytoma.

Brainstem and cerebellum (156, 157)

- CBC and serum biochemistry.
- Screening thoracic and abdominal radiography and ultrasonography to rule out metastatic diseases.
- MRI of the brain is suggested, as CT is less sensitive for detecting soft tissue changes within the caudal fossa due to beam hardening artefacts.
- CSF analysis.
- Infectious disease titres.
- Free T4 by equilibrium dialysis, total T4, thyroid stimulating hormone and other thyroid function testing.

Vestibular system

- CBC and serum biochemistry.
- Screening thoracic and abdominal radiography and ultrasonography to rule out metastatic diseases.
- Otoscopy ± ear swabs.
- Pharyngeal examination (to rule out polyps).
- Bullae radiographs.
- MRI of the brain and peripheral vestibular apparatus is suggested, as it may be challenging to discriminate central from peripheral vestibular disease based on physical examination. CT provides inferior imaging of the caudal fossa due to beam hardening artefacts.
- Myringotomy for cytology and culture of lesions extending into the middle ear.
- CSF analysis if concurrent involvement of central structures is possible.
- Free T4 by equilibrium dialysis, total T4, thyroid stimulating hormone and other thyroid function testing.

Table 50 **Differential diagnoses of ataxia by neuroanatomical localization**

SPINAL CORD

DISEASE MECHANISM	DOGS	CATS
Vascular	Fibrocartilaginous embolism* Vascular malformations Spinal cord haematoma or haemorrhage	Fibrocartilaginous embolism* Vascular malformations Spinal cord haematoma or haemorrhage
Inflammatory/ infectious	Infectious meningomyelitis/myelitis (*Toxoplasma**, *Neospora**, rickettsial, fungal, canine distemper*, rabies) Discospondylitis and spinal epidural empyema Meningomyelitis/myelitis of unknown aetiology (GME)*	Infectious meningomyelitis/myelitis (*Toxoplasma**, feline leukaemia virus myelopathy, FIP*, fungal, rabies) Meningomyelitis/myelitis of unknown aetiology (very rare)
Trauma	Spinal fracture/luxation* Traumatic disc herniation *	Spinal fracture/luxation* Traumatic disc herniation*
Toxic	N/A	N/A
Anomalous	Atlantoaxial subluxation (C1–C5)* Spina bifida Hemivertebra Myelodysplasia Syringo(hydro)myelia* Sub(intra)arachnoid cyst*	Spina bifida (especially Manx) Myelodysplasia
Metabolic	N/A	N/A
Idiopathic	N/A	N/A
Neoplastic	Primary or metastatic spinal column or spinal cord tumour*	Primary or metastatic spinal column or spinal cord tumour*
Nutritional		B12 deficiency Hypervitaminosis A
Degenerative	Intervertebral disc disease* Degenerative myelopathy (T3–L3) Cervical spondylomyelopathy*	Intervertebral disc disease (especially caudal lumbar segments) Storage diseases

* Common cause

FIP = feline infectious peritonitis

N/A = not applicable

(Continued)

Table 50 **Differential diagnoses of ataxia by neuroanatomical localization** (*continued*)

BRAINSTEM (including central vestibular)

DISEASE MECHANISM	DOGS	CATS
Vascular	Brain infarct* Brain haemorrhage*	Brain infarct* Brain haemorrhage*
Inflammatory/ infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial, rabies)* Meningoencephalitis of unknown aetiology (GME, necrotizing, idiopathic)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, rabies)* Meningoencephalitis of unknown aetiology (presumed immune mediated) (very rare)
Trauma	Head trauma*	Head trauma*
Toxic	Metronidazole toxicity*	Metronidazole toxicity*
Anomalous	Intracranial intra-arachnoid cyst Dermoid/epidermoid cyst Dandy–Walker syndrome Chiari-like malformation Hydrocephalus	Intracranial intra-arachnoid cyst Dermoid/epidermoid cyst Hydrocephalus
Metabolic	Hypothyroidism	N/A
Idiopathic	N/A	N/A
Neoplastic	Primary or metastatic brain tumour*	Primary or metastatic brain tumour*
Nutritional	Thiamine deficiency	Thiamine deficiency
Degenerative	Storage diseases Other neurodegenerative disease	Storage diseases Other neurodegenerative disease

CEREBELLUM

DISEASE MECHANISM	DOGS	CATS
Vascular	Brain infarct* Brain haemorrhage	Brain infarct Brain haemorrhage
Inflammatory/ infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial, rabies)* Meningoencephalitis of unknown aetiology (GME, necrotizing)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, rabies)* Meningoencephalitis of unknown aetiology (presumed immune mediated) (very rare)
Trauma	Head trauma	Head trauma
Toxic	Marijuana 5-fluorouracil	Marijuana 5-fluorouracil
Anomalous	Chiari-like malformation* Intracranial intra-arachnoid cyst Cerebellar hypoplasia Dermoid/epidermoid cyst Dandy–Walker syndrome	Cerebellar hypoplasia* Intracranial intra-arachnoid cyst Dermoid/epidermoid cyst

(Continued)

Table 50 **Differential diagnoses of ataxia by neuroanatomical localization** (*continued*)

CEREBELLUM

DISEASE MECHANISM	DOGS	CATS
Metabolic	N/A	N/A
Idiopathic	N/A	N/A
Neoplastic	Primary or metastatic brain tumour*	Primary or metastatic brain tumour*
Nutritional	N/A	N/A
Degenerative	Storage diseases Cerebellar abiotrophy Other neurodegenerative disease	Storage diseases Other neurodegenerative disease

PERIPHERAL VESTIBULAR SYSTEM

DISEASE MECHANISM	DOGS	CATS
Vascular	None	None
Inflammatory/ infectious	Otitis media/interna*	Otitis media/interna* Nasopharyngeal polyp*
Trauma	Head trauma	Head trauma
Toxic	Aminoglycosides* Topical iodophors* Loop diuretics Topical chlorhexidine*	Aminoglycosides* Topical iodophors* Loop diuretics Topical chlorhexidine*
Anomalous	Congenital vestibular disease	Congenital vestibular disease
Metabolic	Hypothyroidism*	N/A
Idiopathic	Acute idiopathic peripheral vestibular disease*	Acute idiopathic peripheral vestibular disease*
Neoplastic	Middle and/or inner ear tumour	Middle and/or inner ear tumour
Nutritional	N/A	N/A
Degenerative	N/A	N/A

* Common cause

FIP = feline infectious peritonitis

N/A = not applicable

COMMON CAUSES OF ATAXIA

The most frequently identified aetiologies responsible for acute-onset ataxia in dogs and cats have been listed in the previous Tables in this chapter and will be reviewed elsewhere in this book. Thiamine deficiency, an often overlooked cause of brainstem signs, will be briefly discussed here.

Thiamine deficiency

Overview

Thiamine deficiency is identified in cats, and, less commonly, in dogs. In these species, thiamine deficiency results in polioencephalomalacia, haemorrhage and necrosis within brainstem nuclei (especially the caudal colliculi and vestibular nuclei). Potential causes include decreased thiamine intake (dietary insufficiency, prolonged anorexia, vomiting) and diseases affecting normal intestinal absorption or interfering with utilization (liver disease, pancreatic disease).

Clinical presentation

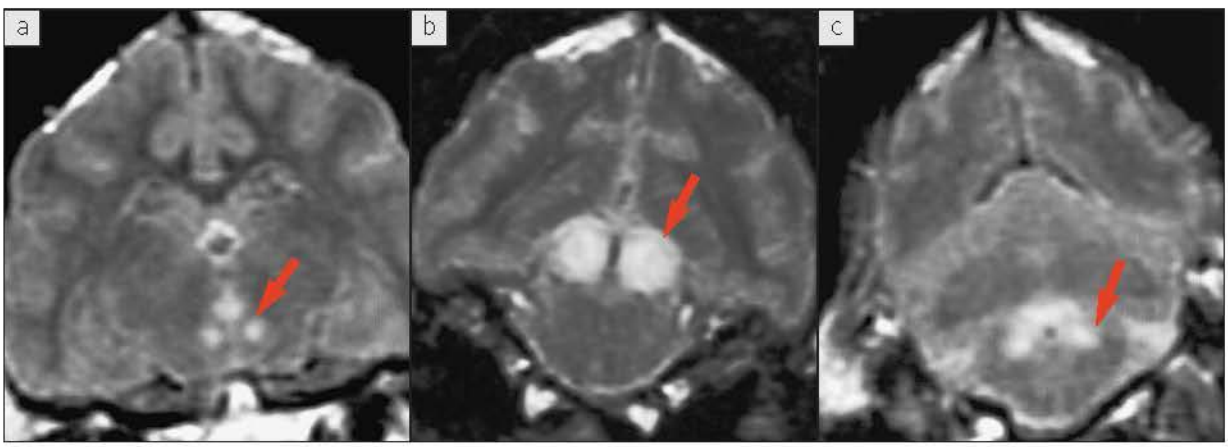
Thiamine deficiency is acute to subacute in onset, with progressive, usually bilateral, neurological deficits including blindness, mydriasis, cervical ventroflexion and vestibular dysfunction. Vestibular and GP ataxia are observed in most cases. Some animals may have additional signs relating to involvement of other body systems (e.g. vomiting and weight loss).

Diagnosis

Diagnosis is based on a combination of brain MRI (bilateral symmetrical brainstem nuclear lesions) (**158**), erythrocyte transketolase levels (where available) and/or urinary organic acid profile (high lactate, 2-hydroxyisovaleric acid, 2-hydroxyadipic acid concentrations). Response to treatment can be considered diagnostic in most cases.

Management

Treatment consists of thiamine supplementation (oral or intramuscular at 25–50 mg q12h for dogs; 10–25 mg q12h for cats) for at least 1 month after clinical signs have regressed and potential diseases affecting utilization/absorption have been corrected. Intramuscular delivery may be preferable in animals with gastrointestinal disease that limits thiamine absorption. Resolution of signs will occur in days to weeks.



▲ **158** T2-weighted MR images of a crossbreed dog with thiamine deficiency showing bilateral symmetrical nuclear hyperintensities (arrowed) at the level of the red nuclei (a), caudal colliculi (b) and vestibular nuclei (c).

ACUTE PARESIS AND PARALYSIS

John McDonnell

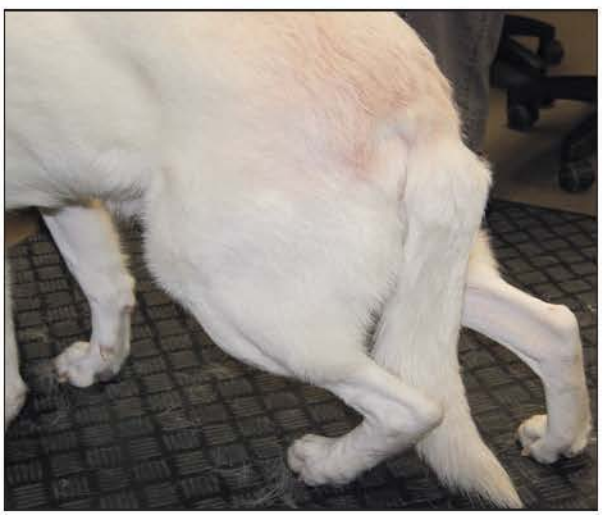
INTRODUCTION

Paresis and paralysis (plegia) are common neurological problems requiring emergency evaluation and treatment. Determining the neurological basis for the paresis and paralysis is an essential goal for the clinician and is necessary to guide the diagnostic and therapeutic decision-making process.

As a general rule, initial evaluation of an animal with a gait abnormality should be done with the aim of determining if the animal is ataxic (uncoordinated), paretic (weak) or lame (from either NM disease or an orthopaedic disorder) and which limb(s) is/are involved. Ataxia is covered in Chapter 9.

In general:

- Paresis is defined as loss of ability to support weight and/or inability to generate a gait; it can be manifested as weakness or decreased strength of voluntary motor movement (**159**), most commonly seen with spinal cord diseases and NM diseases. The term paresis implies that some voluntary movement is still present, as compared with paralysis, which refers to a more severe paresis with complete (-plegia) loss of voluntary movement (**160**). Paresis can be an ambulatory or a non-ambulatory presentation.



▲ **159** Paresis is suggested in this dog by a reduced ability to bear weight in the hindlimbs.



▲ **160** Reduced to absent motor function (paresis to paralysis) is suggested by the posture of this dog.

- Modifying prefixes are used to describe the abnormalities seen. Monoparesis is weakness associated with one limb (**161**), while paraparesis is used to describe weakness confined to the hindlimbs. Tetraparesis (or quadriparesis) is used to describe weakness in all four limbs (**162**). Hemiparesis is weakness confined to a single side of the body (**163**).
- Paralysis (plegia) is substituted for paresis when complete loss of voluntary motor ability is identified.
- GP ataxia and UMN paresis are often seen together with spinal cord disorders due to the close anatomical relationship of the respective sensory and motor pathways.
- Lameness usually presents with a short stride on the affected limb and a long stride on the contralateral limb and is commonly associated with pain from orthopaedic disease. It can also be associated with nervous system dysfunction, referred to as nerve root signature. Lameness can be difficult to differentiate from paresis caused by dysfunction of the lower motor unit. Careful neurological and orthopaedic evaluation is therefore critical to confirm or rule out a neurological basis for the lameness (see Chapter 16).

▼ **161** A 7-year-old mixed breed with left hindlimb monoparesis due to a nerve sheath tumour affecting the lumbar plexus.





▲ **162** A 4-year-old Greyhound cross with weakness in all four limbs due to ischaemic myelopathy.



◀ **163** A young Beagle with left-sided motor dysfunction due to a lateralized cervical disc.

Postural reaction testing should be performed to differentiate between neurological and orthopaedic causes of lameness (**164**). Animals with orthopaedic lameness should not have deficits in proprioceptive placing, hopping, hemistanding or placing reactions. Support may be necessary if significant pain is a component of the presenting complaint. As an example, a dog with a humeral fracture may attempt to replace its paw to the normal position after the paw is knuckled over if the animal is given enough support.

The finding of paresis or paralysis requires accurate lesion localization within the nervous system before an appropriate differential diagnosis can be established and further testing ordered.

▼ **164** **Hopping can assist in the detection of postural reaction abnormalities, confirming neurological disease rather than orthopaedic disease, as long as the dog's body weight is well supported during the procedure.**



NEUROANATOMICAL BASIS

Paresis and paralysis localize the underlying disease to within the neuraxis and/or lower motor units. Within the nervous system, the problem should be further localized as an intracranial problem, spinal cord problem or generalized lower motor unit disease.

The lower motor neuron (LMN) unit is the final common pathway for motor control. It includes the ventral horn cell within the spinal cord or within the CN nucleus of the brainstem and the axon. The ventral root, spinal nerve, peripheral nerve and the individual nerve fibres that innervate the muscle fibres represent the anatomical portions of the axon. The final portion of the LMN unit is the NM junction and the muscle fibres innervated by the axon (see **138**). Activation of the LMN causes contraction of the muscle which it innervates.

The UMN systems include the corticospinal, rubrospinal, reticulospinal, tectospinal and vestibulospinal systems that control the LMN unit, which is the final common pathway of voluntary movement. All of these systems, except the vestibulospinal tract, tend normally to inhibit the LMN. Therefore, when the UMN systems are activated, the LMN is inhibited and the innervated muscle relaxes.

The generation of gait is a complex and delicate balance of the UMN pathways, the LMN system and feedback provided by the GP system. The two major components of gait generation are the postural and protraction phases. Activation or facilitation of the nerves to the anti-gravity extensor muscles provides the postural phase of gait generation. These muscles provide weight support. Protraction is accomplished by facilitation of the neurons that innervate the flexor muscles to initiate movement, in addition to facilitation of the neurons that innervate the extensor muscles to complete the movement. The GP (sensory) system monitors the range, rate and position of the limbs by receptors that are diffusely located throughout the body in muscles, tendons and joints.

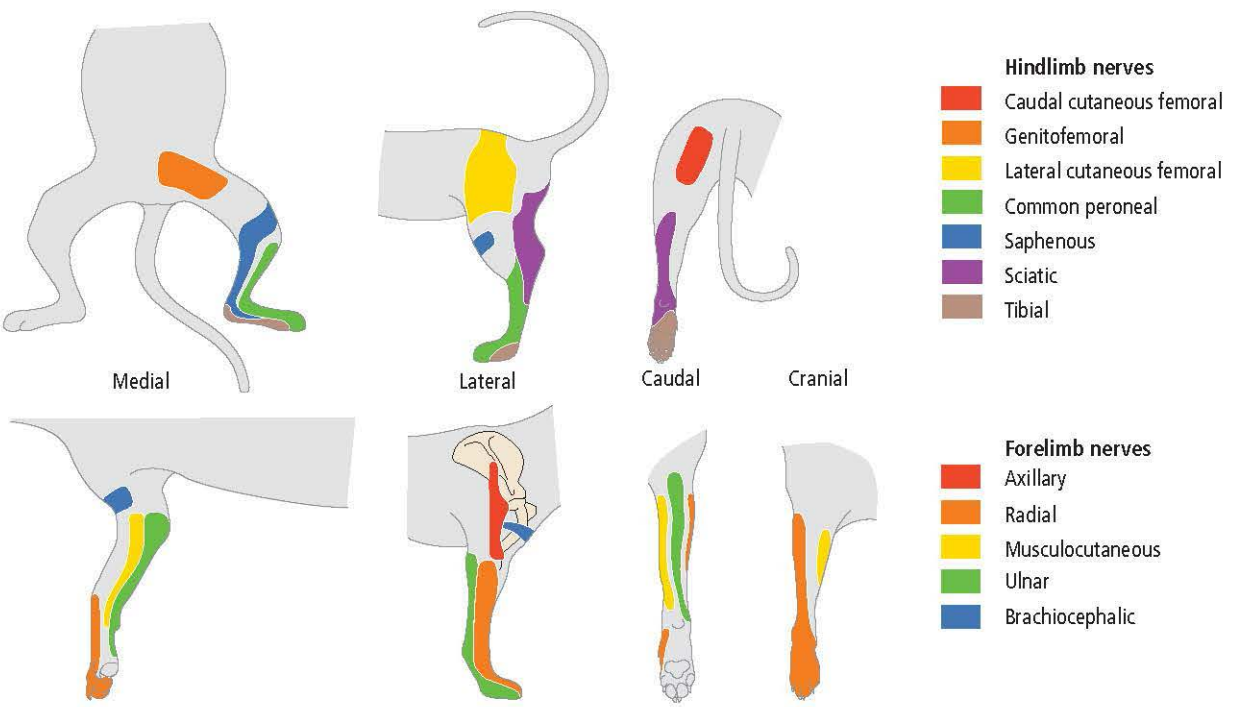
Central gait generators modulate motor neuron activity through a network of interneurons in the spinal cord grey matter. In domestic animals these central gait generators are located in the spinal cord intumescences. A normal gait requires UMN activation and inhibition of the spinal reflex mechanism of the LMN unit. These spinal cord gait generators drive ambulation in domestic

animals as opposed to the corticospinal and cerebral motor cortices in primates. This results in a relatively normal gait in dogs and cats with significant forebrain lesions such as tumours or infarctions.

Voluntary motor movement differs from reflexive movement and muscle tone. It is very important to understand that complete spinal cord transection will leave the LMNs below the site of injury intact and reflexive motor movements can occur. A spinal cord lesion that causes paresis or paralysis can affect both the UMN and LMN systems. Other signs, including muscle tone, myotatic stretch spinal reflexes, withdrawal or flexor reflexes and autonomous zone mapping (**165**), allow more accurate localization than gait evaluation alone (*Table 51*). In animals with LMN paresis and paralysis there is typically reduced tone, reduced strength of reflexes and hypoaesthesia or anaesthesia in the autonomous zone of the spinal nerve's cutaneous innervation. (For further information the reader is directed to Chapter 16.) UMN paresis and paralysis usually result in increased tone, normal or increased reflexes and complete anaesthesia of the affected limbs.

Table 51 **Differentiation between LMN and UMN signs in the neurological examination**

EXAMINATION FINDINGS	LMN SIGNS	UMN SIGNS
Motor function	Paresis or paralysis	Paresis or paralysis
Reflexes	Reduced or absent	Normal to increased
Muscle tone	Reduced	Normal to increased
Hypoaesthesia/ anaesthesia	Distribution isolated to autonomous zones of the spinal nerves affected (**165**)	With complete lesions, there is a more diffuse and generalized anaesthesia of the limbs affected
Muscle atrophy	Rapid and severe atrophy, specifically of muscles innervated by affected nerves	Mild, slow atrophy due to disuse



▲ 165 **Approximate representation of the cutaneous autonomous zones of innervation in dogs and cats.**

NEUROLOGICAL EVALUATION

The finding of paresis or paralysis in the absence of intracranial signs indicates spinal cord disease or generalized LMN unit disease. Brainstem injury is unlikely to cause paralysis without obvious additional signs such as altered states of consciousness, vestibular ataxia, cerebellar ataxia or CN dysfunction. Apart from acute disease processes (i.e. infarct, haemorrhage and head trauma), lesions affecting the forebrain cause contralateral paresis that is so mild it is usually not apparent in the gait.

The next goal for the clinician is to further localize the problem, as diagnostic approaches, differential diagnoses and treatment options differ for each possible disease location.

The neurological evaluation of patients with paresis and paralysis focuses on several critical points.

- What is the motor status of the patient: weak or paralysed?
- Are signs confined to the hindlimbs or are the forelimbs also involved?
- Is one side worse than the other?
- Are the postural reactions in each limb intact or reduced?
- In the abnormal limbs, identify whether the signs are consistent with LMN or UMN dysfunction (*Table 5.1*).
- Is spinal column manipulation associated with discomfort?
- What is the sensory status of the patient? Is there a behavioural response to noxious stimulation of the superficial and deep limb tissues?

The neurological evaluation should be done systematically in a relaxed setting using a neurological examination form to ensure that it is completely undertaken, a permanent record exists and comparisons of serial examinations are possible. Gait and postural reactions identify which limbs are affected, while reflexes, tone and muscle mass evaluation help identify LMN versus UMN signs (*Table 5.1*).

1. Gait evaluation

Initial evaluation of an animal with a gait abnormality should be done with the aim of determining whether the animal is ataxic, paretic or lame (from either NM disease or an orthopaedic disorder) and which limb(s) is/are involved. The locomotor status should be evaluated on a non-slick surface with support if needed (**166**). Asymmetry should be assessed and graded. Assessing weakness can be done by describing whether the animal can rise, stand or walk unassisted. Other semi-quantitative descriptors could include how far it can walk without falling, how much support the animal needs to rise or stand, and how much support is needed for purposeful ambulation. Noting the involvement of forelimbs is important, as some animals with tetraparesis may have marked weakness in the hindlimbs and minimal weakness in the forelimbs.

In ambulatory animals, gait analysis can help differentiate LMN from UMN paresis. LMN dysfunction typically results in a short-strided gait with decreased ability to support weight. Dysfunction of the descending UMN system results in a long-strided, 'reaching' and stiff gait. Animals with a caudal cervical lesion are often described as having a 'two-engine gait' with a short, choppy gait in the forelimbs and a long-strided, floating gait in the hindlimbs.



▲ **166** Sling support, as shown here, may be needed to assess motor function effectively in large and weak dogs.

2. Postural reaction testing

Postural reactions should be evaluated in all animals presenting for paresis and paralysis. Each limb should be evaluated and the results noted on the neurological examination form. The aim of postural reaction testing is primarily to detect subtle abnormalities that were equivocal or not obvious on gait evaluation. The results of gait evaluation and postural reaction testing help to identify which limbs are involved. Muscle tone and segmental spinal reflexes are then tested on each abnormal limb to determine if the lesion is UMN or LMN in nature. Specific postural reaction tests can be selected based on the size and cooperation of the patient (see Chapter 1).

3. Evaluation of musde tone and segmental spinal reflexes

Muscle tone should be assessed by flexing and extending the limb and joints (**167**). Although increased resistance is indicative of UMN signs, it can also be seen in animals that are fractious, excitable or in pain, as well as in association with LMN paresis affecting the flexor system. Diminished tone is a hallmark of LMN signs.

Segmental spinal reflexes should be performed in lateral recumbency with the non-dependent limb being tested. Responses graded as absent or depressed indicate LMN dysfunction, while responses graded as normal or exaggerated indicate UMN dysfunction. Specific spinal reflexes that should be examined include the patellar, flexors (withdrawal) and perineal reflexes. Anal tone should be evaluated by rectal palpation. Other spinal reflexes, such as the triceps, biceps, and gastrocnemius, may be tested, but it should be remembered that these reflexes are inconsistent and therefore unreliable, even in normal animals.

4. Evaluation of tail, bladder and anal sphincter

Tail function is evaluated by assessment of voluntary tail movement, tail tone and sensation. Bladder and urethral function are evaluated by assessment of bladder size, resistance to manual expression and presence of urine dribbling. The bladder is often large, firm and difficult to express with UMN lesions (i.e. lesions cranial to the S1 spinal cord segment), while the bladder is large, flaccid and easily (but incompletely) expressed with LMN lesions (*Table 52*). The anal sphincter is evaluated by assessment of anal tone on digital rectal palpation, presence of anal reflex and sensation (**168**).

5. Sensory testing

Nociception testing is performed with a small haemostat systematically over the surface of the affected limbs. Application of pressure should only be escalated when the initial stimulus fails to elicit a behavioural response such as turning of the head, vocalizing or an escape behaviour.



▲ **167** Increased muscle tone of the forelimbs is seen in this dog, but is best appreciated by attempting to flex and extend all the joints of each limb.



▲ **168** Reduced anal tone is evident in this dog, which had a severe lumbosacral lesion.

6. Cutaneous trunci reflex and spinal palpation/manipulation

The cutaneous trunci reflex enables accurate localization within the T3–L3 UMN spinal cord segments, and additionally assesses the C8–T1 region of the brachial plexus (efferent arm of the reflex) via the lateral thoracic nerve from spinal cord segment C8 or T1. The cutaneous trunci reflex can be decreased or absent caudal to a lesion anywhere in this pathway. In the occasional normal animal the cutaneous trunci reflex is either unreliable or totally absent. This test is conducted by stimulating the skin with a pinprick or by pinching with a pair of haemostats, starting at the iliac crest, about 2.5 cm (1 inch) lateral to the midline. This should result in a bilateral contraction (or twitch) of the cutaneous trunci muscles. In the absence of such muscle contraction, the point of skin stimulation should be moved cranially until a normal reflex is observed (i.e. cut-off point).

Paraspinal palpation is performed near the end of the examination to ensure the continued cooperation of the patient. The clinician should palpate down the spine, feeling for focal pain, muscle spasm and heat. If the dog does not react to light palpation, then moderate pressure is applied. The neck is flexed from side-to-side, dorsally and ventrally, if no pain is elicited on palpation. The lumbosacral junction is flexed and extended while trying not to flex other joints. A repeated behavioural reaction to what should be an innocuous stimulation can be interpreted as pain. Concurrent administration of anti-inflammatory or analgesic medications should be noted, as these may influence the results of the sensory examination.

After collecting and recording the data above, the likely region of the nervous system affected can be identified and specific differential lists can be assembled for appropriate further testing (*Table 53* and **169**, next page).

Lesion localization for paresis and paralysis

- Generalized NM junction diseases and myopathies rarely cause postural reaction deficits because GP pathways are unaffected. Often, decreased strength of the flexor reflex may be the most prominent sign.
- Complete paralysis or non-ambulatory paresis without evidence of intracranial signs, such as mental dullness and CN deficits, is typically due to spinal cord disease.

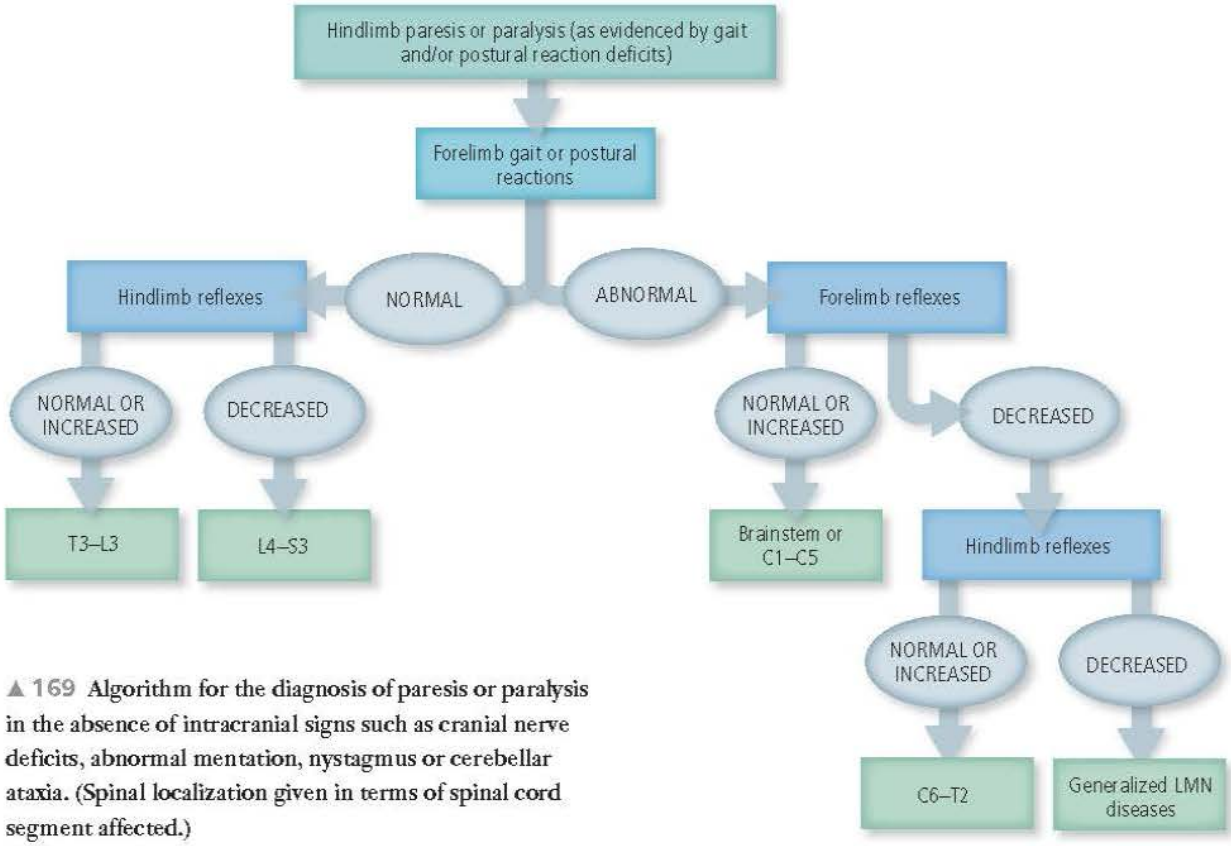
Table 52 **Anatomical and clinical characteristics of UMN and LMN bladder dysfunction**

UMN BLADDER	LMN BLADDER
Lesion cranial to the S1 segment	Lesion caudal to the S1 segment
Conscious voiding attempts usually absent	Conscious voiding attempts absent
Bladder expression difficult	Bladder easily expressed
Large bladder	Half-full to large flaccid bladder
Perineal tone and reflex present	Perineal tone and reflex reduced to absent
May get overflow incontinence when the bladder becomes over-distended	Frequent urine dribbling

- Animals with suspected or documented displaced spinal fractures should be immediately stabilized externally using a backboard (see Chapter 21). Immediate evaluation of the patient should be confined to reflexes and sensory evaluation prior to imaging.
- Spinal pain when present can be a helpful localizer, although some stoic animals may not show obvious pain on palpation. In some of these animals, abdominal 'splinting' (thoracolumbar localization) or resistance to flexion/extension (cervical or cervicothoracic localization) is noted in response to palpation and manipulation. Other potential causes of pain on palpation can include intra-abdominal pathology and orthopaedic pain from the shoulder and hip.
- Nociception testing requires observation of a behavioural response to a noxious stimulus. It is tested by pinching the digits with the fingers or with haemostats, heavy needle holders or even pliers. The response seen may be a turn of the head or vocalization or an escape behaviour. The withdrawal reflex must not be mistaken for a behavioural response. To avoid confusion, the withdrawal reflex should be evaluated first and then increased pressure applied to evaluate pain perception.

Table 53 A summary of neurological examination findings related to spinal cord localization

	SPINAL CORD SEGMENT AFFECTED					
	C1–C5	C6–T2	T3–L3	L4–S3	S1–3	DIFFUSE LMN DISEASE
Gait	Tetraparesis/plegia; hemiparesis/plegia; monoparesis/plegia	Tetraparesis/plegia; hemiparesis/plegia; monoparesis/plegia	Paraparesis/plegia; monoparesis/plegia	Paraparesis/plegia; monoparesis/plegia	Typically normal	Normal to generalized weakness
Forelimb reflexes	Normal to increased	Decreased (especially withdrawal)	Normal	Normal	Normal	Decreased
Hindlimb reflexes	Normal to increased	Normal to increased	Normal to increased	Decreased to absent	Typically normal	Decreased
Urethral and anal sphincter tone	Normal	Normal	Normal	Normal to decreased	Decreased	Normal to decreased
Bladder function	UMN bladder	UMN bladder	UMN bladder	Variable	LMN bladder	Variable



▲ 169 **Algorithm for the diagnosis of paresis or paralysis in the absence of intracranial signs such as cranial nerve deficits, abnormal mentation, nystagmus or cerebellar ataxia. (Spinal localization given in terms of spinal cord segment affected.)**

- The presence or absence of nociception and duration of this sign provide valuable prognostic information about compressive spinal cord lesions. Function often deteriorates with increasing compression, but this is also related to the speed and chronicity of compression. Loss of function develops in a predictable manner in the following sequence: (1) loss of postural reactions, (2) loss of voluntary motor function, (3) loss of superficial pain sensation and (4) loss of deep pain perception. Animals with loss of nociception after disc herniation are reported to have an approximately 60% chance of recovery if surgically decompressed within 48 hours of onset. Animals with loss of deep pain perception following exogenous trauma have a much worse prognosis.
- In non-compressive spinal cord lesions, such as seen with infiltrative spinal cord tumours, vascular infarctions or inflammatory/infectious myelopathies, there is not the same predictable loss of function as seen with compressive spinal cord lesions. Loss of function is expected to be related to the part of the spinal cord affected by the lesion. Some focal spinal cord lesions, such as fibrocartilaginous embolic myelopathy, have shown some anatomical correlation with functional spinal cord areas.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis list depends on the neuroanatomical localization and the presence of a painful focus, as well as the history and signalment of the patient. Although a presumptive diagnosis may be made based on the most common disease to affect a specific patient, it is best to develop a complete differential list to confirm or exclude less likely diseases. Any time that a patient is not progressing as expected, the differential list should be revisited and re-evaluated.

Diseases and conditions commonly necessitating the emergency evaluation of a dog or cat with paresis and paralysis are outlined in *Tables 54–56* (pp. 214–216).

Specific diagnostic tests

The choice of neurodiagnostic tests in animals with paresis and paralysis depends on the neurolocalization, severity of signs and, often, the availability of diagnostic modalities. Many tests require specialized skills and equipment to perform and interpret. They are also not without risks to the animals and these risks should be discussed with the animal's owner.

Spinal cord localization (C1–S3)

- Minimum database including CBC, serum chemistry analysis and urinalysis. Based on the results of the physical examination, a thyroid evaluation may be needed.
- Spinal radiographs: ventrodorsal and lateral radiographs of the previously identified neuroanatomical spinal location. Animals should be sedated prior to radiographic examination. In animals with suspected vertebral fractures or luxations, extreme care should be exercised.
- Spinal imaging, such as myelography, CT or MRI, requires anaesthesia and specialized skills and equipment for performance (see Chapter 4).
- CSF collection and analysis. CSF needs to be collected prior to injection of myelographic contrast into the subarachnoid space and should be analysed rapidly to prevent degradation of the cells. This should usually be avoided if trauma cannot be ruled out.

Lower motor neuron unit disease

- Minimum database consisting of CBC, chemistry profile, urinalysis and T4.
- Further laboratory work may be indicated based on results of the examination and minimum database (endocrine testing, infectious disease titres, toxin screening).
- Edrophonium testing if MG suspected (see Chapter 24).
- Serum testing for anti-acetylcholine receptor antibodies if MG suspected (see Chapter 24).
- Electrodiagnostic testing, such as EMG, motor nerve conduction studies, sensory nerve conduction studies, repetitive nerve stimulation testing, single-fibre EMG and F-waves studies. These tests require anaesthesia, special equipment and specialized skills to perform and interpret.

Table 54 **Causes of acute paresis and paralysis**

	TETRAPARESIS/PLEGIA LOCALIZED TO C1–T2	PARAPARESIS/PLEGIA LOCALIZED TO T3–L3
DISEASE MECHANISM	EXAMPLES	EXAMPLES
Vascular	Fibrocartilaginous embolism* (D, rare C) Vascular malformations Spinal cord haematoma or haemorrhage	Fibrocartilaginous embolism* (D, rare C) Vascular malformations Spinal cord haematoma or haemorrhage
Inflammatory/infectious	Meningo(encephalo)myelitis (viral, bacterial, rickettsial, protozoal, fungal or immune mediated)* Discospondylitis*/osteomyelitis Spinal epidural empyema	Meningomyelitis (viral, bacterial, rickettsial, protozoal, fungal or immune mediated)* Discospondylitis*/osteomyelitis Spinal epidural empyema
Trauma	Spinal fracture/luxation* Traumatic disc herniation*	Spinal fracture/luxation* Traumatic disc herniation*
Toxic	None	None
Anomalous	Atlanto-axial subluxation* Syringo(hydro)myelia	Syringo(hydro)myelia
Metabolic	None	None
Idiopathic	None	None
Neoplastic	Primary or metastatic spinal column or spinal cord tumour*	Primary or metastatic spinal column or spinal cord tumour*
Nutritional	Hypervitaminosis A (C)	Nutritional hyperparathyroidism Hypervitaminosis A (C)
Degenerative	Intervertebral disc disease* Cervical spondylomyelopathy* (D)	Intervertebral disc disease*

LOWER MOTOR NEURON UNIT CAUSES OF ACUTE PARESIS AND PARALYSIS

(See Part 3, Chapters 17 to 28, for the specific causes of UMN paresis and paralysis.)

Polyradiculoneuritis or Coonhound paralysis

Overview

Polyradiculoneuritis is seen in dogs and rarely in cats. It can be seen 7–10 days following a raccoon bite or exposure to other immunological stimulus. The lesion involving the ventral roots and peripheral nerves is composed of demyelination and mononuclear interstitial infiltrate. This disease is probably immune mediated, although treatment with corticosteroids does not influence the course of the disease.

Clinical presentation

There is an acute onset of a flaccid paraparesis rapidly ascending to involve the forelimbs. CNs are typically normal, although facial weakness and dysphonia can be noted. Megaoesophagus is not a feature of this disease. The perineal reflex is normal and urinary continence is maintained. In the early stages of the disease, hyperaesthesia can be seen. Recurrent episodes are possible.

PARAPARESIS/PLEGIA LOCALIZED TO L4–S3	
EXAMPLES	
Fibrocartilaginous embolism* (D, rare C) Aortic thromboembolism Vascular malformations Spinal cord haematoma or haemorrhage Ascending and descending haemorrhagic myelomalacia	
Meningomyelitis (viral, bacterial, rickettsial, protozoal, fungal or immune mediated)* Discospondylitis*	
Spinal fracture/luxation* Traumatic disc herniation*	
None	
Syringo(hydro)myelia	
None	
None	
Primary or metastatic spinal column or spinal cord tumour*	
Endocrine neuropathies Hypervitaminosis A (C)	
Intervertebral disc disease*	

* Common cause; C = cats; D = dogs

Table 55 **Causes of generalized or diffuse neuromuscular diseases seen on emergency evaluation****

DISEASE MECHANISM	EXAMPLES
Vascular	None
Inflammatory/infectious	Polyradiculoneuritis* Myasthenia gravis* Polymyositis Polyneuritis
Trauma	None
Toxic	Tick paralysis* (D) Botulism* Aminoglycoside toxicity Coral snake envenomation Organophosphate toxicity
Anomalous	None
Metabolic	Endocrine polyneuropathies
Idiopathic	Acquired myasthenia gravis Necrotizing myopathy (D)
Neoplastic	Paraneoplastic polyneuropathy
Nutritional	None
Degenerative	None

* Common cause; C = cats; D = dogs

** See also Chapter 8

Diagnosis

Diagnosis is based on clinical signs and exclusion of other acute LMN diseases (e.g. botulism, MG and tick paralysis ± adrenal insufficiency and electrolyte imbalance). Electrodiagnostic tests, such as EMG and motor nerve conduction velocity (MNCV), are abnormal, but these changes are not evident until 5–7 days after onset. CSF analysis may show elevated protein and a normal cell count and cytology (albumino-cytological dissociation).

Management

Excellent supportive care, including cleaning, frequent turning, physical rehabilitation and expressing the bladder, is required for animals that have severe signs. Vigilant monitoring for urinary tract infections, pneumonia and bed sores, with immediate aggressive treatment, will assure good outcomes. Respiratory paralysis may result if the phrenic nerve and intercostal nerves are severely affected and may require ventilatory support. The overall course of the disease is typically 6 weeks, although cases lasting 4–6 months are not uncommon.

The prognosis for recovery is good if respiratory failure does not occur and supportive care is aggresive.

Table 56 **Differentiaton of the most common causes of acute diffuse neuromuscular diseases**

	POLYRADICULO-NEURITIS	TICK PARALYSIS	BOTULISM	MYASTHENIA GRAVIS–ACQUIRED
Signalment and history	Any breed or age. Some dogs have a history of raccoon bites (hunting dogs) or other immunostimulation. Can be acute onset or progress from hind-limbs to forelimbs	Any breed with potential exposure to ticks. Signs occur 5–7 days after tick bite. Tick is typically still attached at time of clinical sign	Any breed or age. History includes rubbish or carcass ingestion with onset of signs hours to days. Multiple cases are suggestive	Congenital (3–8 weeks). Acquired (bimodal age distribution). Can be acute in onset, but more typically episodic or exercise-induced weakness
Clinical signs	Typically progresses from a hindlimb paresis to tetraparesis/ tetraplegia over 4–5 days. Does not involve tail, sphincters or cranial nerves except for some dogs showing mild facial paresis and voice changes. Animals can have severe flaccid paralysis, but mental status is normal, often wagging tail	Rapid progression from first signs to recumbency (24–48 hours). Rarely involves cranial nerves	Rapid progression of clinical signs. Can be accompanied by gastrointestinal signs. Cranial nerve deficits including gag, facial droop, swallowing and megaoesophagus are common	Acute signs (fulminant) or exercise-induced weakness (fatigable) involving palpebral reflexes, facial nerve, weak gag, laryngeal paresis or paralysis, dysphagia and megaoesophagus. Spinal reflexes are often preserved
Electrodiagnostics	EMG. Fibrillation potentials and positive sharp waves 3–7 days after signs develop. Conduction velocity reduced and dispersed. Increased F-wave latency and F-ratio	EMG usually normal. Conduction velocity normal or slightly decreased. Evoked potentials reduced	EMG usually normal. Conduction velocity normal. Evoked potentials reduced. Repetitive nerve stimulation can be slow	EMG usually normal, but minor changes can be seen. Conduction velocity normal, but decremental response with repetitive nerve stimulation. Single-fibre EMG shows typical 'jitter'
Diagnosis	Diagnosis by exclusion	Identification and removal of tick should result in clinical signs resolving	Toxin in stomach contents, serum or faeces can be identified with a bioassay	Anti-acetylcholine receptor antibody titre. Edrophonium (Tensilon) test can be supportive
Treatment and prognosis	Supportive care; may require ventilator support. 4–6 weeks recovery is typical	Complete resolution of signs 24–72 hours after tick removed	Supportive care; may require ventilator support. 1–3 week recovery	Anticholinesterase drugs ± immunosuppressive drugs and supportive care. Prognosis guarded, but worsens dramatically if aspiration pneumonia and megaoesophagus develop

Aortic thrombosis or ischaemic neuromyopathy secondary to aortic thromboembolism

Overview

This condition occurs commonly in cats with hypertrophic cardiomyopathy and occasionally in dogs with hypercoagulable states.

Clinical presentation

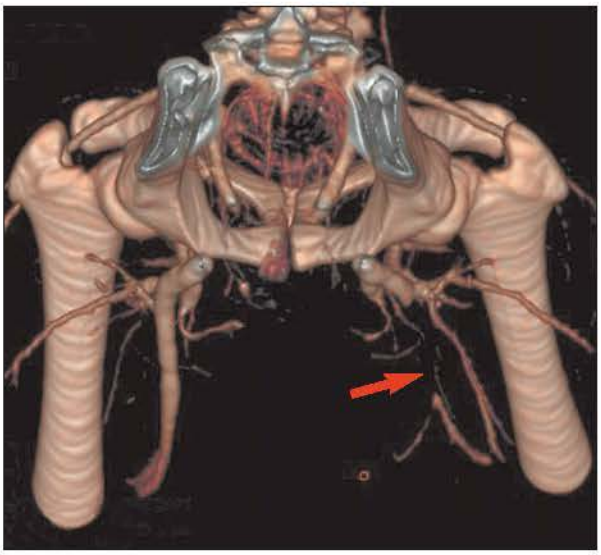
The typical presentation is a middle-aged to geriatric animal with an acute onset of hindlimb pain and paralysis with no progression. The exact clinical signs relate to the region of circulatory obstruction. Other signs of circulatory compromise are typically seen, including cool, pale or cyanotic extremities and lack of arterial pulses. A history of ongoing signs of hypertrophic cardiomyopathy in cats is usually evident.

Diagnosis

Other conditions, such as sepsis, neoplasia, heart disease including heartworm infection, immune-mediated haemolytic anaemia and protein-losing nephropathy or enteropathy, are uncovered with a basic investigation including a minimum database. Advanced imaging, such as CT (**170**) and MRI, as well as Doppler ultrasonography, is necessary to identify vascular compromise.

Management

Treatment is aimed at treating the primary cause of the thrombus formation, removing the obstruction and decreasing the continued accumulation of the thrombus. A recent report on the use of tissue plasminogen activator in 11 cats with arterial thromboembolism documented a high rate of side-effects (11/11) and a low rate of hospital discharge (3/11). Although some animals will functionally recover, recurrence is likely if treatment of the underlying disease is not addressed.



▲ **170** **A 3D reconstructed CT scan in cross-section at the level of the pelvic inlet of a dog with aortic trifurcation thrombosis. Absence of femoral artery structure detected by the CT can easily be seen on one side (arrow). (Photo courtesy Davies Veterinary Specialists)**

Tick paralysis

See Chapter 28.

Snake envenomation

See Chapter 28.

Botulism

See Chapter 25.

Acquired myasthenia gravis

See Chapter 24.

SPINAL PAIN

Ronaldo da Costa

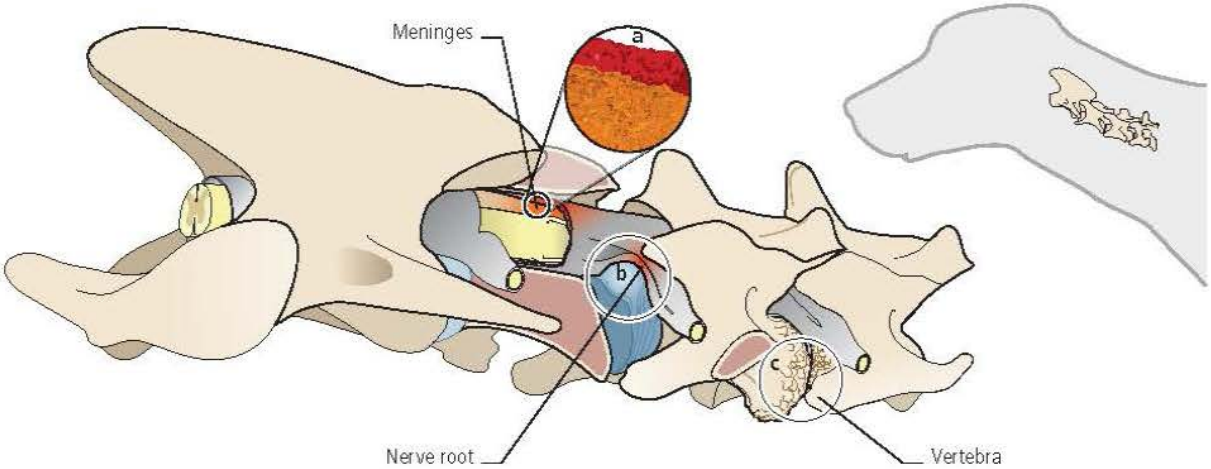
INTRODUCTION

Spinal pain is a common clinical sign associated with a variety of neurological conditions. In some diseases it is the most prominent feature, while in others it is less obvious, but equally important. The approach to a patient with spinal pain is similar to that for other neurological presentations. First, a physical examination is performed to investigate the presence of systemic signs, such as fever, followed by a neurological examination to allow identification of other neurological problems and to localize the lesion(s). With this information, the clinician can then establish the differential diagnoses and select the most appropriate test(s) to rule in or rule out a specific diagnosis. The presence of spinal pain associated with neurological deficits helps the clinician narrow down the list of differential diagnoses, because some spinal diseases can be broadly classified as painful diseases (e.g. meningitis, disc extrusion, discospondylitis or extramedullary spinal tumour) or as non-painful diseases (e.g. ischaemic myelopathy). The presence of neurological signs is important to rule out joint disease (polyarthritis) and muscle disease (polymyositis).

NEUROANATOMICAL BASIS OF SPINAL PAIN

Spinal pain reflects the involvement of at least one of three main structures: meninges, vertebrae (vertebral periosteum) and nerve roots or spinal nerves (**171**). The presence of spinal pain is relatively consistent when a disease process affects these structures. However, many different disease mechanisms can cause pain when these structures are affected. In dogs and cats the most common mechanisms leading to spinal pain are inflammation (e.g. meningitis, discospondylitis), compression (e.g. intervertebral disc extrusion compressing the nerve roots) and destruction or lysis (e.g. vertebral neoplasia).

▼ 171 Cranial cervical spine of a dog demonstrating the three most common structures (meninges, nerve roots, and periosteum) responsible for causing spinal pain in dogs and cats: (a) representation of inflamed meninges as seen in cases of meningitis; (b) lateralized intervertebral disc protrusion causing nerve root compression; (c) periosteal changes secondary to discospondylitis. (Image courtesy Ohio State University)



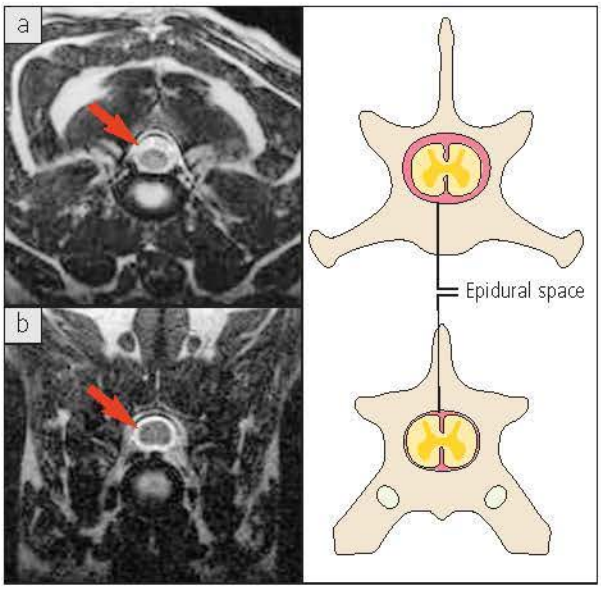
Other less common sources of spinal pain in small animals are intervertebral disc degeneration (discogenic pain), arthritic changes affecting the vertebral facet joints and dysplasia of the caudal vertebral facets. Unlike in humans, disc degeneration and arthritis rarely cause spontaneous spinal pain in dogs and cats. Before attributing spinal pain to disc degeneration or to spinal arthrosis or arthritis, it is necessary to rule out other more common causes of pain affecting the meninges, vertebrae or nerve roots. Spondylosis is a non-inflammatory degenerative process affecting the bone (vertebral body); it is rarely associated with spinal pain and should not cause neurological signs. Disseminated idiopathic skeletal hyperostosis (DISH) is a more severe form of spondylosis, but should also not cause spontaneous pain or neurological deficits. Spondylosis or DISH should never be considered to be the cause of spinal pain or neurological deficits without a thorough diagnostic work-up ruling out all other causes of spinal pain.

Spinal pain in the thoracolumbar area is frequently associated with neurological deficits, while in the cervical region it can commonly be the only clinical sign. The reason for this clinical difference is that there is a larger vertebral canal in the cervical region in comparison with the thoracic or lumbar regions. This allows a larger area for the cervical vertebral canal to accommodate compressive lesions. The so-called 'cord-to-canal' ratio is also different between the cranial and caudal cervical regions. The caudal cervical vertebral region has the cervicothoracic enlargement of the spinal cord and, as such, less space to accommodate compressive lesions. Thus, caudal cervical lesions tend to be associated more commonly with neurological deficits (e.g. cervical spondylomyelopathy) in comparison with cranial cervical lesions (e.g. intervertebral disc disease) (**172**).

While the meninges, periosteum and epineurium have a high density of nociceptors, the spinal cord parenchyma does not contain nociceptors. Because of this, strictly myelopathic diseases, such as degenerative myelopathy or fibrocartilaginous embolic myelopathy, are not associated with spinal pain.

There are basically three types of pain: physiological, inflammatory and neuropathic. Physiological pain serves as a protective mechanism, warning animals of damaging stimuli. Inflammatory pain occurs in response to tissue damage and stimulation of mechanosensitive, chemosensitive and thermosensitive nociceptors. Inflammatory pain usually improves with the use of anti-inflammatory drugs. Neuropathic pain is characterized by abnormal somatosensory processing in the PNS or CNS. It is usually manifested as paraesthesia (abnormal sensation without any physical cause) or allodynia (increased pain from stimuli that are not normally painful). One of the best examples of a cause of neuropathic pain in veterinary medicine is Chiari-like malformation and syringomyelia, particularly in dogs with a large syrinx and dorsal horn involvement.

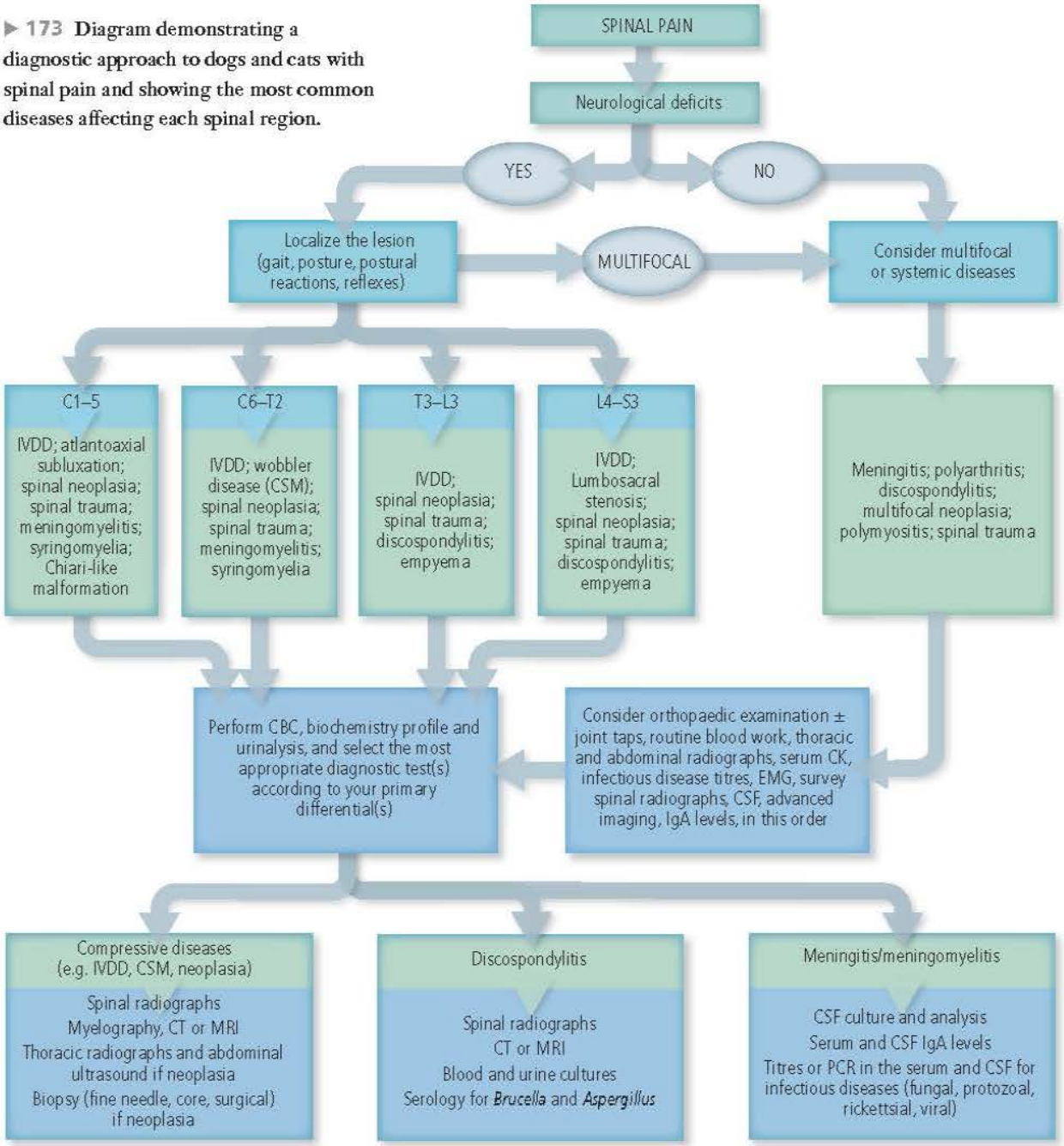
Rarely, intracranial diseases can cause cervical pain. The neck pain seen in these cases may reflect the involvement of thalamic structures (thalamic pain syndrome) or distension of the meningeal nerve endings caused by a space-occupying intracranial lesion. Other signs suggestive of thalamocortical dysfunction (abnormal behaviour, decreased menace response and/or nasal sensation) can be very relevant for the purpose of lesion localization in these cases.



▲ **172** **Magnetic resonance imaging of a 7-year-old, clinically normal male Doberman Pinscher. (a) Cervical spinal cord at C2/3. Observe the bright signal around the spinal cord (arrow) within the larger vertebral canal. (b) Cervical spinal cord at C6/7. Observe the spinal cord (arrow) and the smaller epidural space surrounding it compared with the C2/3 region.**

NEUROLOGICAL EVALUATION

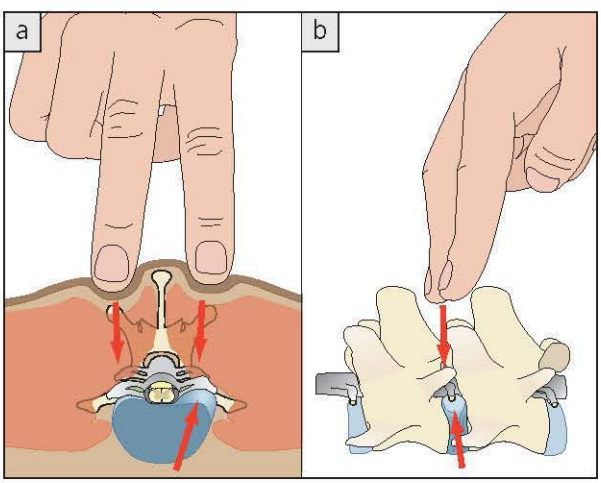
Dogs and cats with spinal pain may present with or without neurological signs. Lesion localization and diagnostic approach are facilitated when the patient shows obvious signs of spinal pain (e.g. kyphosis, ventroflexed neck) or when the owner is aware of the location of the spinal pain. The neurological examination is then aimed at confirming the presence of spinal pain, localizing it precisely (either focal or multifocal) and assessing the extent, if any, of neurological involvement (**173**). Occasionally, spinal pain may be episodic, with the patient only showing signs of pain for a few seconds or minutes. On neurological examination, there may be no



▶ **173 Diagram demonstrating a diagnostic approach to dogs and cats with spinal pain and showing the most common diseases affecting each spinal region.**

evidence of spinal pain detected. It is best to re-evaluate these patients after a few hours to days, depending on the duration of presentation, and/or ask the owner for a video recording of these episodes at home before proceeding with further diagnostics. Frequently, these events of severe episodic pain are due to cervical disease. Dogs with thoracolumbar and lumbosacral pain have more consistent signs of pain that can often be elicited on spinal palpation.

A complete neurological examination (evaluation of mental status, gait and posture, CNs, postural reactions, spinal reflexes and spinal palpation) should always be performed in patients with spinal pain to establish the location(s) of the lesion(s). Gait evaluation is the most important component of the examination with regard to establishing the presence of neurological deficits. Proprioceptive ataxia associated with spinal pain indicates the concurrent presence of spinal cord disease (myelopathy). Care should be exercised in the interpretation of postural reactions (hopping, proprioceptive positioning) in dogs and cats with severe spinal pain, since they may appear to have delayed responses due to severe pain and thus exhibit an unwillingness to respond appropriately. The same may hold true for the CN tests that evaluate thalamocortical function. Severe pain often causes a decreased nasal sensation response and/or menace response, but if this is truly related to pain and stress, it should always be bilateral and symmetric, because both are cortically mediated responses. Spinal palpation should be performed (carefully) at the end of the neurological examination to ensure patient cooperation during the initial parts of the examination. Proper technique is essential to obtain reliable results (**174**). The patient should be supported under the pelvic region and pressure should be applied in a downward fashion between each spinous process, with two fingers equidistant on each side of the process. The goal is to place pressure at the level of the intervertebral foramina, where the spinal nerves exit. In a dog with a disease that causes nerve-root compression (e.g. intervertebral disc herniation), applying pressure in this manner should consistently elicit focal spinal pain. Since spinal problems occur less frequently in the cranial thoracic region in comparison with the lumbosacral and lumbar regions, the clinician can establish the patient's tolerance to spinal palpation by starting the palpation in the cranial thoracic region between the scapulae. This technique often allows specific identification of the painful area when pain is present within regions T2 to L7/S1. The lumbosacral region can be additionally evaluated specifically by lifting the base of the tail and pushing it cranially. This manipulation is suggested to change the angle of the sacrum and the L7 joint and it allows pain to be confirmed in the lumbosacral area without manipulation of the hip joint. Evaluation of the patient in lateral recumbency may also reduce the confounding effects of concurrent joint pain in the limbs. The cervical spine can be evaluated by applying bilateral digital pressure to the transverse processes and intervertebral foramina. Voluntary range of motion can be assessed if no pain is detected.



◀ **174** **(a) Transverse image of the lumbar spine demonstrating the position of the fingers for thoracolumbar spinal palpation. Both fingers should be equidistant and pressure should be applied in a downward fashion. The fingers should be positioned close to the midline, aiming for pressure at the level of the intervertebral foramina. (b) Lateral image of the lumbar spine demonstrating that pressure is applied between the spinal processes where the intervertebral foramina and nerve roots are located. Lateralized intervertebral disc protrusion is seen on both images causing lateralized nerve-root compression. (Image courtesy Ohio State University)**



▲ 175 Typical posture of a Beagle-cross with cervical spinal pain secondary to aseptic suppurative meningoarteritis.



▲ 176 Kyphotic thoracolumbar posture of a mixed breed dog with intervertebral disc extrusion between vertebrae L2 and L3.

SPECIFIC FEATURES OF SPINAL PAIN ACCORDING TO LOCATION

Cervical pain

The presence of cervical pain can often be established by the patient's posture. Dogs and cats with neck pain have restricted cervical movement and a head-down posture (**175**). They have a tendency to follow objects with their eyes rather than with the head. Reluctance to walk may also be observed. If neck pain is evident, cervical manipulations (flexion, extension) are not necessary to ascertain the presence of pain, and can lead to neurological deterioration if spinal instability is present. Cervical palpation (digital palpation over the vertebral bodies and intervertebral foramina) can be used to localize areas of pain or muscle spasms and are safer to perform than manipulations. The author prefers to use food to assess the voluntary range of motion in all four directions (dorsal, ventral, right and left lateral) rather than use forced cervical manipulations.

Occasionally, a combination of cervical pain and forelimb lameness is observed. This has been called 'nerve root signature' and usually is seen with lesions in the caudal cervical spine involving the nerve roots or spinal nerves.

It is not uncommon for cervical pain to have an episodic character. It is the author's impression that these episodic presentations of neck pain are usually associated with nerve root/spinal nerve involvement. Another cause of spontaneous pain is the neuropathic pain seen in dogs with Chiari-like malformation and syringomyelia. These episodic presentations are in contrast to the more constant and less episodic pain seen when meninges and osseous structures are affected.

Thoracolumbar pain

Owners of small breed dogs can usually perceive the presence of spinal pain when they pick up their dogs, or by their dog's reluctance to go upstairs or jump up or down. Thoracolumbar pain may be more difficult to detect in large breed dogs. Acute thoracolumbar pain usually leads to a kyphotic (arched) thoracolumbar posture (**176**). The location of the kyphotic region (thoracic, thoracolumbar or lumbar) can facilitate localization of the area of spinal pain by the clinician. Chronic thoracolumbar pain does not usually lead to a kyphotic posture.

Table 57 **Possible causes of spinal pain in dogs and cats**

DISEASE MECHANISM	DOGS	CATS
Vascular	Epidural haemorrhage	Epidural haemorrhage
Inflammatory/infectious	Discospondylitis (bacterial or fungal)* Meningitis (aseptic suppurative meningo-arteritis* or bacterial meningitis) Infectious meningomyelitis (bacterial, fungal, rickettsial, viral)* Non-infectious meningomyelitis (GME)* Spinal epidural empyema Vertebral osteomyelitis Polyarthritis Polymyositis	Discospondylitis Meningitis Infectious meningomyelitis Non-infectious meningomyelitis Vertebral osteomyelitis Polyarthritis Polymyositis
Trauma	Spinal trauma (fracture/luxation)* Traumatic atlantoaxial subluxation Traumatic disc herniation	Spinal trauma (fracture/luxation)* Traumatic atlantoaxial subluxation Traumatic disc herniation
Toxic	None	None
Anomalous	Atlantoaxial subluxation* Chiari-like malformation and syringomyelia Multiple cartilaginous exostoses Sacrocaudal dysgenesis Dermoid sinus	Atlantoaxial subluxation Multiple cartilaginous exostoses
Metabolic	None	None
Idiopathic	Arachnoid cyst	Arachnoid cyst
Neoplastic	Primary or secondary spinal tumours* Intracranial tumours (rare)	Primary or secondary spinal tumours* Intracranial tumours (rare)
Nutritional	Pathological fractures due to metabolic bone disease	Hypervitaminosis A Pathological fractures due to metabolic bone disease
Degenerative	Intervertebral disc degeneration* Cervical spondylomyelopathy* Degenerative lumbosacral stenosis* Osteochondrosis dissecans of lumbosacral joint Degenerative osteoarthritis of articular facets (facet dysplasia) Extradural synovial cysts Calcinosis circumscripta	Intervertebral disc degeneration Degenerative osteoarthritis of articular facets Degenerative lumbosacral stenosis Extradural synovial cysts

* Common cause

Lumbosacral pain

The presence of lumbosacral pain often is perceived by the owners, but sometimes can be confused with orthopaedic (hip) pain. Historically, evidence of lumbosacral pain includes difficulty getting up or sitting down, a reluctance to jump up into the car or go upstairs, and pain when touched in the caudal lumbar region. In addition, the tail may be 'down' and the dog may not wag its tail as it used to. A guarded lumbar/lumbosacral posture with kyphosis may be seen in more acute cases. Occasionally, the pain may be worse after exercise, a feature not seen with cervical or thoracolumbar pain. Lumbosacral pain may be the only clinical sign or it may be associated with other signs such as weakness (paresis) or lameness, which can be suggestive of nerve root or spinal nerve compression. Many dogs with lumbosacral disease have concurrent orthopaedic problems, such as hip dysplasia or cranial cruciate ligament rupture. It is very important to evaluate the lumbosacral region specifically by lifting the tail and pushing it cranially, isolating it from the hip joint.

DIFFERENTIAL DIAGNOSIS

Conditions to be considered when evaluating a dog or cat presented with spinal pain are listed in *Tables 57* and *58*.

Diagnostic tests

The ancillary tests should be selected according to lesion localization and differential diagnoses. For example, spinal radiographs can sometimes be very useful, but are not recommended for cases of suspected meningitis.

- **CBC and biochemistry profile.** May reveal evidence of inflammatory (infectious or non-infectious) diseases and changes suggestive of neoplasia, but can all be completely normal in the presence of a markedly inflammatory CNS process.
- **Urinalysis/urine culture.** Can allow identification of a source of chronic infection and the infectious agent in cases of discospondylitis or empyema.
- **Survey radiographs.** Allows assessment of osseous spinal structures. It is useful to rule out major structural lesions as seen with discospondylitis, osteomyelitis or vertebral tumour. Absence of abnormalities cannot rule out spinal lesions. Proper positioning is essential.
- **Thoracic and abdominal imaging.** Useful to rule out primary or secondary neoplastic processes.
- **CSF analysis**. Essential to confirm an inflammatory process in the CNS. Aim to collect the CSF caudal to the location of the lesion. The type of pleocytosis can assist the clinician in establishing an aetiological diagnosis (see Chapters 4 and 19).
- **Arthrocentesis and joint fluid analysis.** May confirm the presence of polyarthritis. Young, large breed dogs may have concurrent immune-mediated polyarthritis and meningitis.
- **Myelography.** Outlines the spinal cord structure. It allows indirect visualization of extradural, intradural/extramedullary and intramedullary lesions.
- **CT**. Can be used alone or with intravenous or subarachnoid contrast (myelography) to enhance visualization of lesions.
- **MRI.** Is the gold standard technique for investigating diseases affecting the spinal cord. Allows visualization of the spinal cord parenchyma and provides superior sensitivity when compared with other imaging techniques.
- **Scintigraphy.** May be used in cases of non-localized pain.
- **Biopsy.** Surgical biopsy of muscle or bone can assist in the identification of neoplastic or inflammatory conditions.
- **Serum and CSF titres/PCR for infectious diseases.** Used to confirm specific infectious diseases causing myelitis/meningomyelitis.
- **Blood and urine culture.** Potentially useful for cases of discospondylitis.

Table 58 **Conditions that may mimic spinal pain**

- Polyarthritis
- Polymyositis
- Paraspinal muscle abscess
- Abdominal conditions (pyelonephritis, pancreatitis)
- Pelvic conditions (prostatic abscess)
- Bilateral cranial cruciate ligament rupture

COMMON CAUSES OF SPINAL PAIN

Discospondylitis and vertebral osteomyelitis (spondylitis)

Overview

Discospondylitis and vertebral osteomyelitis (spondylitis) are infections of the intervertebral disc and adjacent endplates (discospondylitis) or vertebral body (spondylitis). The most commonly encountered infectious agents are coagulase-positive staphylococci (*S. aureus*, S. *intermedius*), *Streptococcus* spp., *Brucella canis* and *E. coli*. Fungal (*Aspergillus* spp., *Blastomyces dermatitidis*, *Histoplasma capsulatum*, *Coccidioides immitis*, *Paecilomyces*) or *Actinomyces* spp. (secondary to grass awn) are rare in comparison. The conditions are more common in male, large and giant breed dogs and are rare in cats and small, chondrodystrophic dogs.

Haematogenous spread from distant sources (e.g. skin, heart valves, oral cavity, urinary tract, testes, prostate, uterus) is the most common form of infection. It can be secondary to penetrating wounds, foreign bodies (grass awn migration, gunshot pellets), epidural analgesia or disc fenestration during spinal surgery.

Clinical presentation

Clinical signs consist of severe (sometimes diffuse) spinal pain, often without neurological deficits initially. Affected dogs and cats may present with systemic illness, but can be normothermic and systemically normal. The conditions can occur anywhere along the spine, but are more common at the L7–S1 and T13–L1 regions, and the thoracic spine.

With progression of the disease, degeneration of the disc can lead to disc protrusion/extrusion, causing signs of myelopathy. Less commonly, infection spreading to the epidural space can cause spinal epidural empyema; infection spreading to the meninges can also cause meningitis.

Diagnosis

Diagnosis is based on the radiographic features of collapse of disc space with endplate lysis and sclerosis. Radiographic changes may not occur for 10–14 days after onset of infection. CT or MRI can be used and are more sensitive for earlier stages of infection, with MRI also assisting with the identification of soft tissue changes and investigation of associated foreign bodies.

Radionuclide bone imaging can be used when a definitive diagnosis cannot be reached on survey radiographs. It is usually abnormal before bone lysis becomes evident on survey radiographs. Changes consist of increased uptake of radiopharmaceutical at the affected disc space and endplates. However, caution should be used when interpreting the natural age-related degeneration seen particularly at the LS joint, which will also result in increased radiopharmaceutical uptake.

Investigation of a potential systemic infectious focus should be considered in all cases. This may involve dental examination, thoracic radiographs and heart and abdominal ultrasound for endocardial and prostatic or renal disease, respectively.

Culture of blood, urine or disc/bone material should be performed to identify the causative organism. Serology for *Brucella* also should be performed, especially in intact animals in endemic regions.

Management

Treatment of discospondylitis is difficult and prolonged (2–4 months); relapses are not uncommon. Ideally, treatment should be guided by the results of culture and sensitivity. Cephalosporin antibiotics are a good empiric choice initially. Intravenous antibiotics should be considered if severe neurological compromise is present. Empirical treatment can be initiated after all samples (urine, blood, disc aspirate) have been taken for culture and sensitivity. If there is no response within 5 days, the antibiotics should be changed or a better sample should be obtained from the infected disc either at surgery or under fluoroscopy.

Cage rest is important to minimize the risk of pathological fracture or luxation. Analgesia should be provided using non-steroidal and/or other analgesics. Corticosteroids are contraindicated.

Surgery is indicated if there is no response to medical treatment or to provide decompressive surgery in patients with substantial neurological deficits and compression identified on imaging. Surgical stabilization may be necessary in some cases and can prove to be successful even when infection has not been completely resolved.

Spinal epidural empyema (epidural abscess)

Overview

Epidural empyema or abscess is a suppurative, septic process within the epidural space of the vertebral canal. It can be the result of haematogenous spread, vertebral osteomyelitis, discospondylitis, paraspinal muscle abscessation or direct inoculation of bacteria (e.g. following a bite or spinal surgery).

Clinical presentation

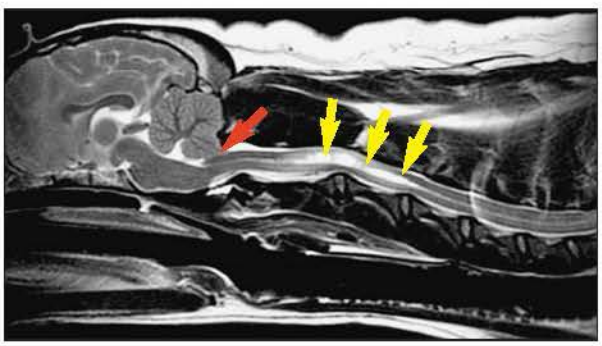
Systemic signs, such as anorexia, lethargy and fever, are common. Most dogs and cats present with spinal pain and neurological deficits.

Diagnosis

Diagnosis is based on haematological findings (neutrophilia), CSF changes (typically neutrophilic pleocytosis with increased protein) and imaging finding of extradural spinal cord compression. Cultures from blood, CSF and surgical material should be performed. A variety of organisms have been reported. Blood and surgical cultures offer the highest diagnostic yield.

Management

Treatment is based on antibiotic therapy along with emergency surgical decompression and abscess drainage. The prognosis is guarded and depends on the degree of neurological impairment and how quickly treatment is instituted.



▲ **177** Sagittal MR image of Chiari-like malformation and syringomyelia in a 2-year-old Cavalier King Charles Spaniel. Note the cerebellar herniation (red arrow) and syringomyelia (yellow arrows) within the cervical spinal cord.

Chiari-like malformation and syringomyelia (caudal occipital malformation syndrome)

Overview

Chiari-like malformation is a disease characterized by a congenital malformation of the occipital bone, resulting in overcrowding of the caudal fossa, abnormal CSF dynamics and subsequent syringomyelia. The most commonly affected breeds are the Cavalier King Charles Spaniel, Brussels Griffon, Yorkshire Terrier and Toy Poodle, with affected dogs usually between 6 months and 3 years old, but the disease is seen in many small and toy breeds of any age.

Clinical presentation

Cervical pain (hyperaesthesia) is the most consistent sign, although sometimes the pain may be difficult to localize. Scratching of the neck and/or shoulder area, typically on one side, is a common sign. Scoliosis, paresis and ataxia may also be seen.

Diagnosis

Diagnosis is established by MRI of the caudal fossa and the cervical spine (**177**).

Management

Medical treatment consists of corticosteroids (prednisone, 0.5 mg/kg PO q24–48h), furosemide (2 mg/kg PO q12h), omeprazole (0.5–0.1 mg/kg PO q24h) and/or gabapentin (10–20 mg/kg PO q8–12h). For refractory cases, pregabalin (2–4 mg/kg PO q8–12h) can be given. Surgical treatment (suboccipital decompression and C1 dorsal laminectomy) is indicated for dogs that respond poorly to medical treatment.

Spinal neoplasia

Overview

Spinal tumours can be located in the extradural, intradural–extramedullary or intramedullary regions. The most common tumours are osteosarcoma and fibrosarcoma in dogs, lymphoma and osteosarcoma in cats. Spinal neoplasia occurs in any breed or age, but large breed dogs (>18 kg) >5 years of age are overrepresented. Lymphoma tends to occur more commonly in young cats (median 4.2 years), while all other feline spinal tumours are seen in older cats (median 9.9 years). Spinal tumours can affect any spinal region, but commonly are found in the cranial thoracic and cervical regions.

Clinical presentation
Clinical signs vary according to tumour location, but spinal pain is a common feature with most spinal neoplasms. Affected dogs may appear with a chronic progressive history, although subacute presentations (fast deterioration over 1–3 days) are very common. The majority of cats have a chronic progressive history. Occasionally, acute onset of spinal pain and myelopathy may result from pathological fracture.

Diagnosis
A minimum database with CBC, biochemistry profile, thoracic radiographs and abdominal ultrasound should always be performed to investigate for systemic primary lesions. Diagnosis is confirmed using spinal radiographs, myelography, CT or MRI (**178**). Biopsy is necessary to establish the tumour type and plan appropriate treatment.

Management
Chemotherapy, radiation therapy and surgery can be used alone or in combination, depending on the tumour type, with varying prognosis. Median survival ranges from a few months (e.g. spinal osteosarcoma) to almost 2 years (e.g. multiple myeloma with chemotherapy).



▲ **178** Dorsal MR image of a 7-year-old mixed breed dog with a spinal meningioma. Observe the circular contrast-enhancing mass (arrow) at C2/C3 on the right side.

Feline hyperaesthesia syndrome
Overview
Feline hyperaesthesia syndrome (FHS), also known as 'rippling skin disease', is a poorly understood condition of cats that may have neurological, NM or behavioural causes. Cats of any age or breed may be affected.

Clinical presentation
Affected cats are extremely sensitive to touch in the lumbar and lumbosacral regions, and may exhibit rippling of the skin over the thoracolumbar area, muscle spasms, compulsive licking and biting at the back, flank and tail, and abnormal erratic behaviour. Neurological deficits are not observed in these cats.

Diagnosis
A presumptive diagnosis is based on history and physical and neurological examination findings. Other spinal diseases need to be ruled out. EMG and muscle biopsies from epaxial muscles can be performed. A behavioural evaluation is often recommended.

Management
Treatment should be directed at the underlying cause, if identified. Usually, cats are treated with anticonvulsants (phenobarbital, 2–3 mg/kg PO q12h or gabapentin, 10–15 mg/kg PO q12h), corticosteroids (prednisolone, 0.5 mg/kg q12–24h), non-steroidal anti-inflammatory drugs (NSAIDs; e.g. meloxicam or piroxicam) or behaviour-modifying drugs (fluoxetine, 0.5–4.0 mg/cat PO q24h; amitriptyline, 2 mg/kg PO q24h; clomipramine, 1–5 mg/cat PO q12–24h). Environmental enrichment may be helpful.

Atlantoaxial subluxation
See Chapter 21.

Acute disc disease
See Chapter 22.

Meningomyelitis, meningitis
See Chapter 19.

Spinal trauma
See Chapter 21.

ACUTE BLINDNESS

Peter Nghiem
& Scott Schatzberg

INTRODUCTION

Acute visual loss or blindness is a relatively uncommon, but important, clinical syndrome of dogs and cats. Bumping into walls or inanimate static objects and an inability to recognize moving objects are classic signs of visual loss that typically are noted by owners of animals with bilateral blindness. However, unilateral blindness may be more difficult for owners to recognize. Depending on the aetiology, visual loss initially may be partial or complete. Partial visual loss may progress to complete blindness over days to weeks. Visual loss may be due to a lesion of the retina, optic nerve, optic chiasm, optic tract, lateral geniculate nucleus (LGN), optic radiations or visual cortices. Although the entire visual pathways are part of the CNS, in this chapter they are divided into:

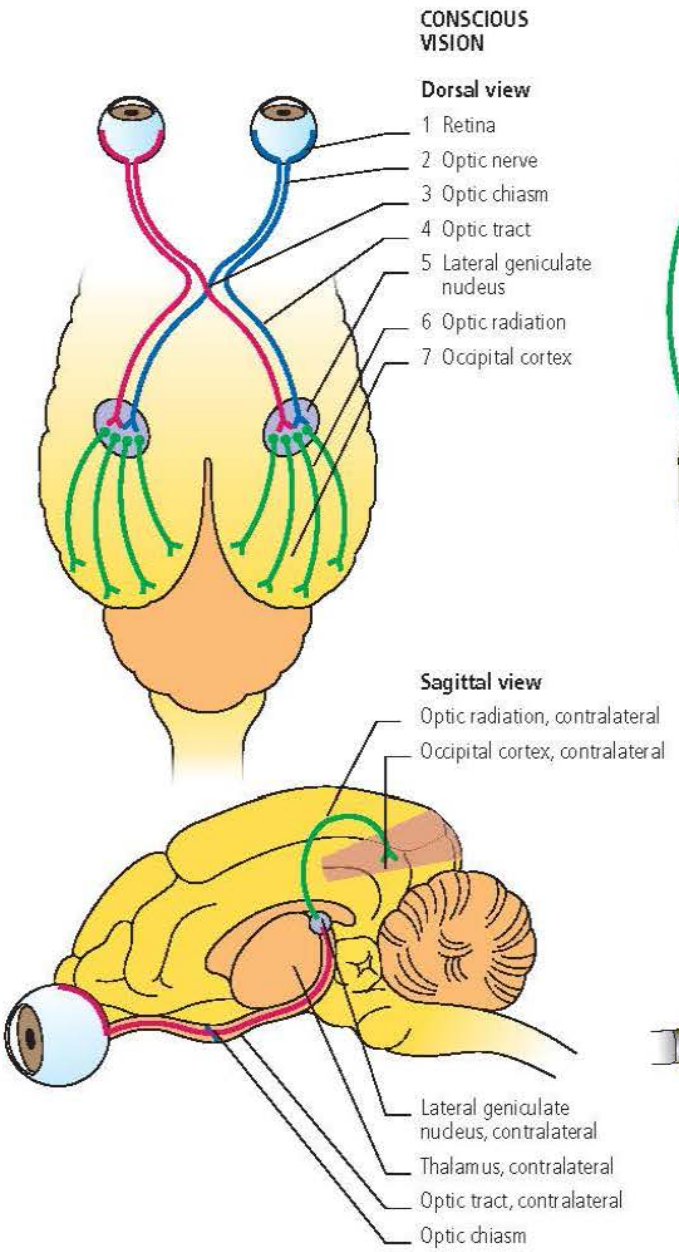
- Peripheral visual pathways: visual pathways that are shared with the PLR pathways (i.e. retina, optic nerve, optic chiasm, proximal optic tract).
- Central visual pathways: distal optic tract, LGNs, optic radiations, visual cortices.

An animal with acute visual loss requires a complete neurological examination to help localize the problem to either the peripheral or the central visual pathway. An accurate neuroanatomical localization allows the clinician to formulate an appropriate differential diagnosis list, to select diagnostic tests and, ultimately, to implement targeted therapies for the disorder responsible for the blindness.

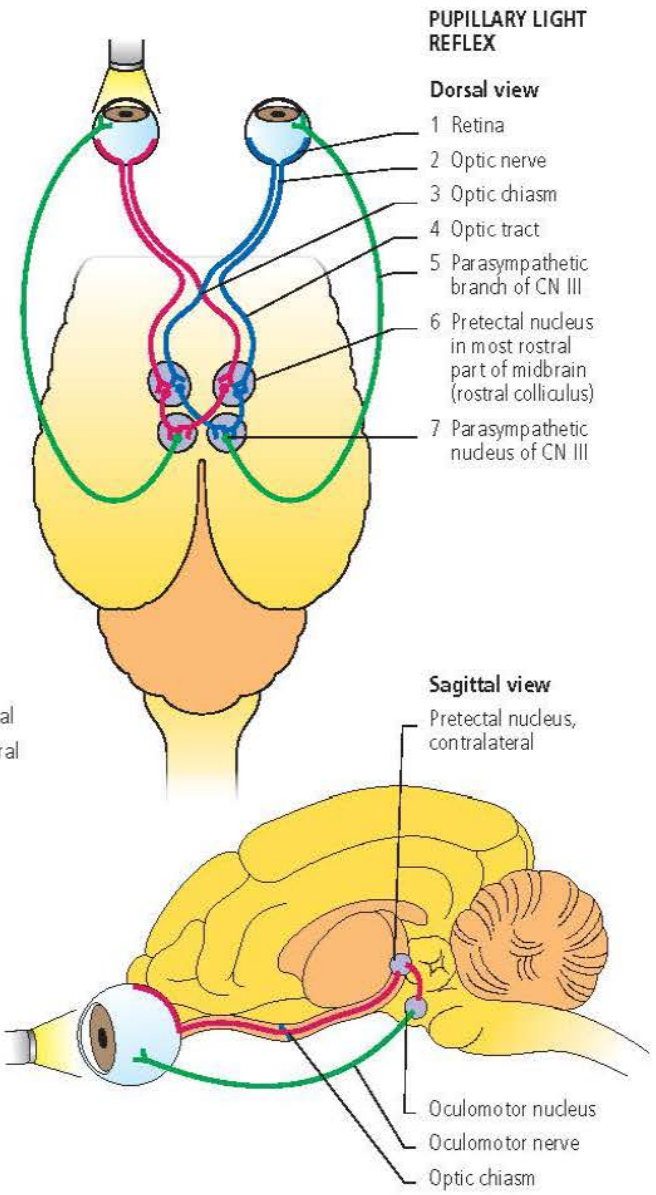
RELEVANT NEUROANATOMY

The visual system is a special sensory system used to relay information to the higher centres of the brain for processing and interpretation. This system consists of the retina, optic nerves, optic chiasm, optic tracts, LGNs, optic radiations and visual cortices (occipital cortices).

Visual stimuli initiate impulses by specialized cells (e.g. photoreceptor cells, bipolar cells) within the retina that are transmitted subsequently to retinal ganglion cells. The axons of retinal ganglion cells transmit impulses to the brain via the optic nerves, which course caudally in the orbit surrounded by meninges, extraocular muscles and periorbita. The optic nerves enter the skull via optic canals of the presphenoid bone and join at the optic chiasm, ventral to the rostral aspect of the hypothalamus and rostral to the pituitary gland. At the optic chiasm, the majority of axons in each optic nerve cross (75% in the dog, 60% in the cat) to form the contralateral optic tract. These axons ultimately influence the contralateral occipital lobes of the cerebral hemispheres. The optic tracts course caudodorsolaterally over the side of the diencephalon to the LGN of the thalamus. When the optic tract reaches the level of the LGN, two basic pathways continue: a pathway for conscious visual perception (~80% of optic tract axons) and a separate pupillary reflex pathway (~20% of optic tract axons).



▲ 179 **Neuroanatomical pathway for conscious vision.** The visual stimulus enters through the retina (1), travels through the optic nerve (2) and optic chiasm (3) – where the majority of fibres (65–75%) cross over – and continues along the optic tract (4). The stimulus is relayed from here to the lateral geniculate nucleus of the thalamus (5), then travels through the optic radiations (6), synapsing in the visual cortex (7). A lesion in any part of this pathway can affect conscious vision.



▲ 180 **Neuroanatomical pathway for the pupillary light reflex (PLR).** A bright light stimulus enters the retina (1) and travels through the optic nerve (2), optic chiasm (3) and optic tract (4). The stimulus is relayed to the pretectal nucleus within the rostral colliculus (6). The parasympathetic nucleus of cranial nerve III (7) is stimulated and the signal is transmitted through its parasympathetic branch (5), resulting in contraction of the iris sphincter muscle and constriction of the pupil. A lesion in any part of the pathway can disrupt the PLR.

For the conscious visual pathway (**179**), axons from neuronal cell bodies of the LGN project caudally as the optic radiations, which terminate in the cerebral (visual) cortex of the occipital lobe. The occipital cortex is where integration and interpretation of visual stimuli occur. Two reflex pathways also exist, one for the PLR and another associated with somatic motor responses to retinal activity.

- For the PLR, approximately 20% of the optic tract axons bypass the LGN and synapse on the pretectal nucleus (PTN) of the midbrain. Some of these fibres synapse on the ipsilateral parasympathetic oculomotor nucleus (CN III), but the majority of the PTN axons cross to synapse on the contralateral parasympathetic oculomotor nerve nucleus (ipsilateral to stimulated eye). Thus, light entering one eye will allow for constriction of both pupils, stronger in the stimulated eye (**180**).
- For somatic responses to retinal activity, some optic tract axons synapse on cell bodies located in the rostral colliculi of the midbrain. Some of these neurons send axons to CNs III, IV and VI and influence 'reflex movement' of the eyes in response to visual input. In addition, other neurons of the rostral colliculi send axons down the spinal cord (tectospinal tract) that influence the LMNs of the cervical spinal cord. The tectospinal tracts are important in activation of muscles concerned with orientation of the head and neck in response to visual input.

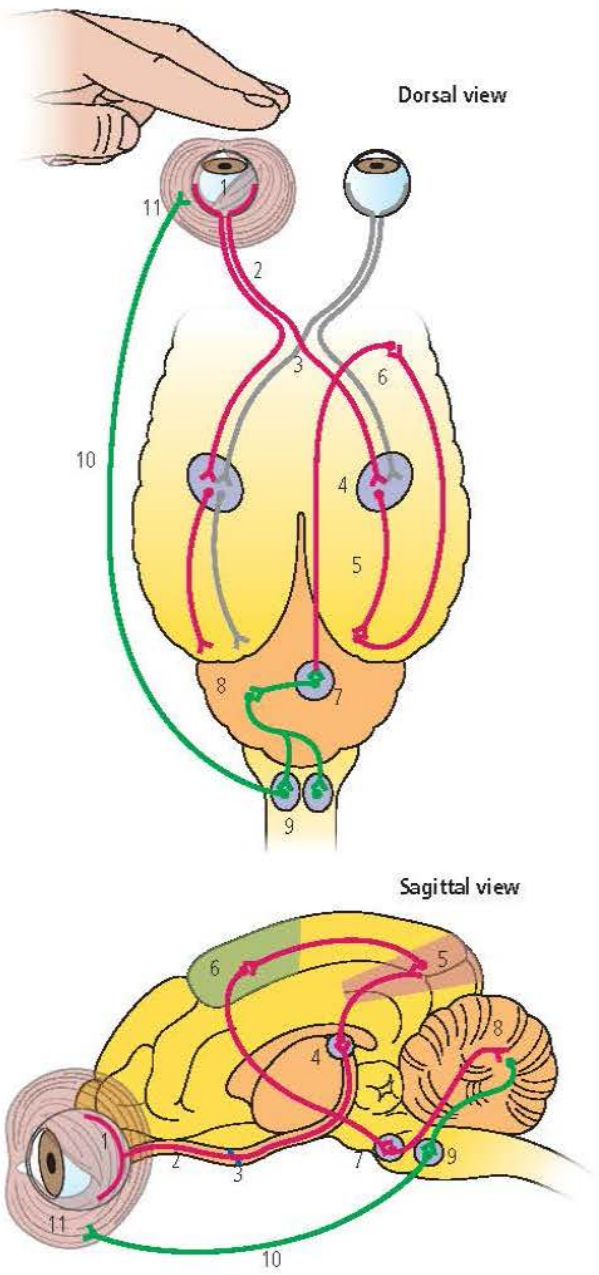
NEUROANATOMICAL LOCALIZATION

Clinical evaluation of a suspected blind animal

Since animals with visual deficits may have a lesion anywhere along the peripheral or central visual pathway, it is imperative that the clinician performs a neurological and fundoscopic examination. In order to localize blindness as peripheral or central, the clinician should carefully evaluate the following:

- A **fundoscopic examination** may disclose changes in retinal reflectivity, vasculature and the optic discs (neuritis or papilloedema). Optic neuritis may result in unilateral or bilateral changes to the optic nerve head (papillitis), including ill-defined edges and displacement of the optic disc. Retinal haemorrhage, vascular attenuation, increased tapetal reflectivity and exudates also may be visualized. Lesions in the retina or optic disc are consistent with a peripheral visual problem. Fundoscopic examination may also reveal papilloedema, which results from oedema tracking down the optic nerve to the optic disc. Optic nerve tumours, although uncommon, may be appreciated as an enlarged optic disc and may also be accompanied by retinal haemorrhage or detachment.
- The **palpebral reflex** should ideally be evaluated before the menace response. The lateral and medial canthus of each eye should be touched separately and a blink response with complete closure of the palpebral fissures should be expected. An intact facial nerve is required for the menace response, palpebral reflexes and dazzle reflex, as it is responsible for orbicularis oculi muscle contraction closing the palpebral fissures.

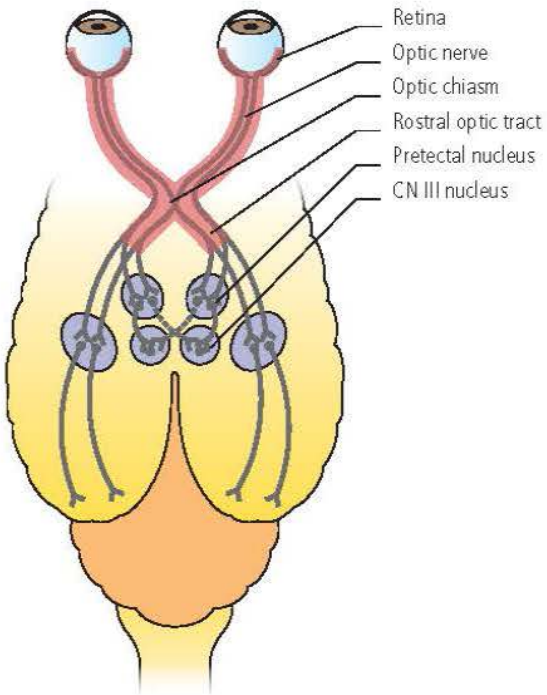
- The **menace response** (**181**) is performed with a menacing gesture of the hand towards one eye, while the other eye is covered; immediate closure of the eyelid is the normal response. This learned response requires the entire peripheral and central visual pathway in addition to connections from the cerebrum (through several theoretical pathways involving the ipsilateral cerebellum) to the ipsilateral brainstem facial neuron.



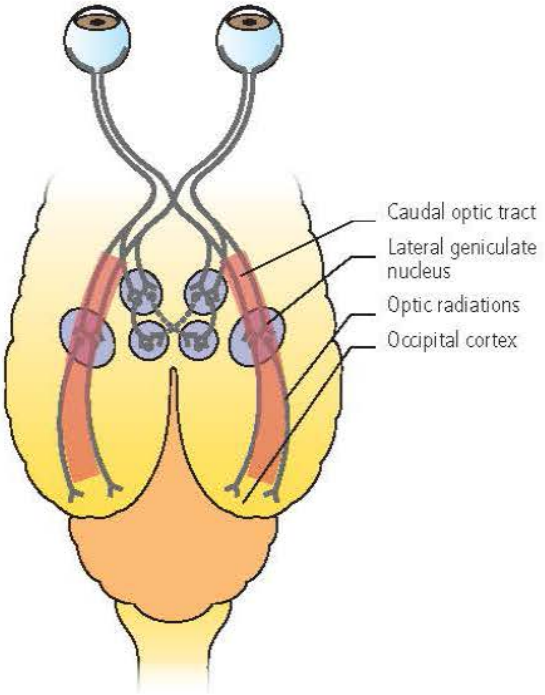
- **PLRs** are tested by directing a bright light towards the lateral retina, which should result in constriction of both pupils. PLR testing evaluates the visual pathway up to the level where optic tract axons bypass the lateral geniculate nucleus to synapse on the PTN (i.e. peripheral visual pathways) and the parasympathetic nuclei of CN III, bilaterally. No involvement of any component of the cerebrum occurs in this reflex (**180**). However, testing the PLRs is important to help distinguish if the lesion is affecting the peripheral or central visual pathways (**182, 183**).

◀ **181** **Neuroanatomical pathway for the menace response. The menacing stimulus is detected by the retina (1) and a resulting impulse travels through the optic nerve (2) and optic chiasm (3) to the contralateral optic tract. The stimulus is relayed to the lateral geniculate nucleus of the thalamus (4), travels through the optic radiation and synapses in the occipital cortex (5). The signal then travels rostrally in association with interneurons and synapses in the motor cortex (6) and continues within projection fibres through the internal capsule, crus cerebri and longitudinal fibres of the pons and synapses in the pontine nucleus (7). It then proceeds within transverse fibres of the pons, through the middle cerebellar peduncle and synapses in the cerebellar cortex (8). The signal travels through the efferent cerebellar pathway and synapses on both facial nuclei (9). It is finally relayed through the left and right facial nerves (only one shown in diagram, 10), synapsing on facial muscles (orbicularis oculi) (11) to cause muscular contraction of the eyelids. A lesion in any part of the pathway can disrupt this response.**

1 Retina
2 Optic nerve
3 Optic chiasm
4 Lateral geniculate nucleus
5 Occipital cortex
6 Motor cortex
7 Pontine nucleus
8 Cerebellar cortex
9 Facial nucleus
10 Facial nerve (CN VII)
11 Orbicularis oculi



▲ 182 **Peripheral visual pathways (outlined in red). These include the retinas, optic nerves, optic chiasm and the rostral portions of the optic tracts.**



▲ 183 **Central visual pathways (outlined in red). These include the caudal aspects of the optic tracts, the lateral geniculate nuclei and the occipital cortices.**

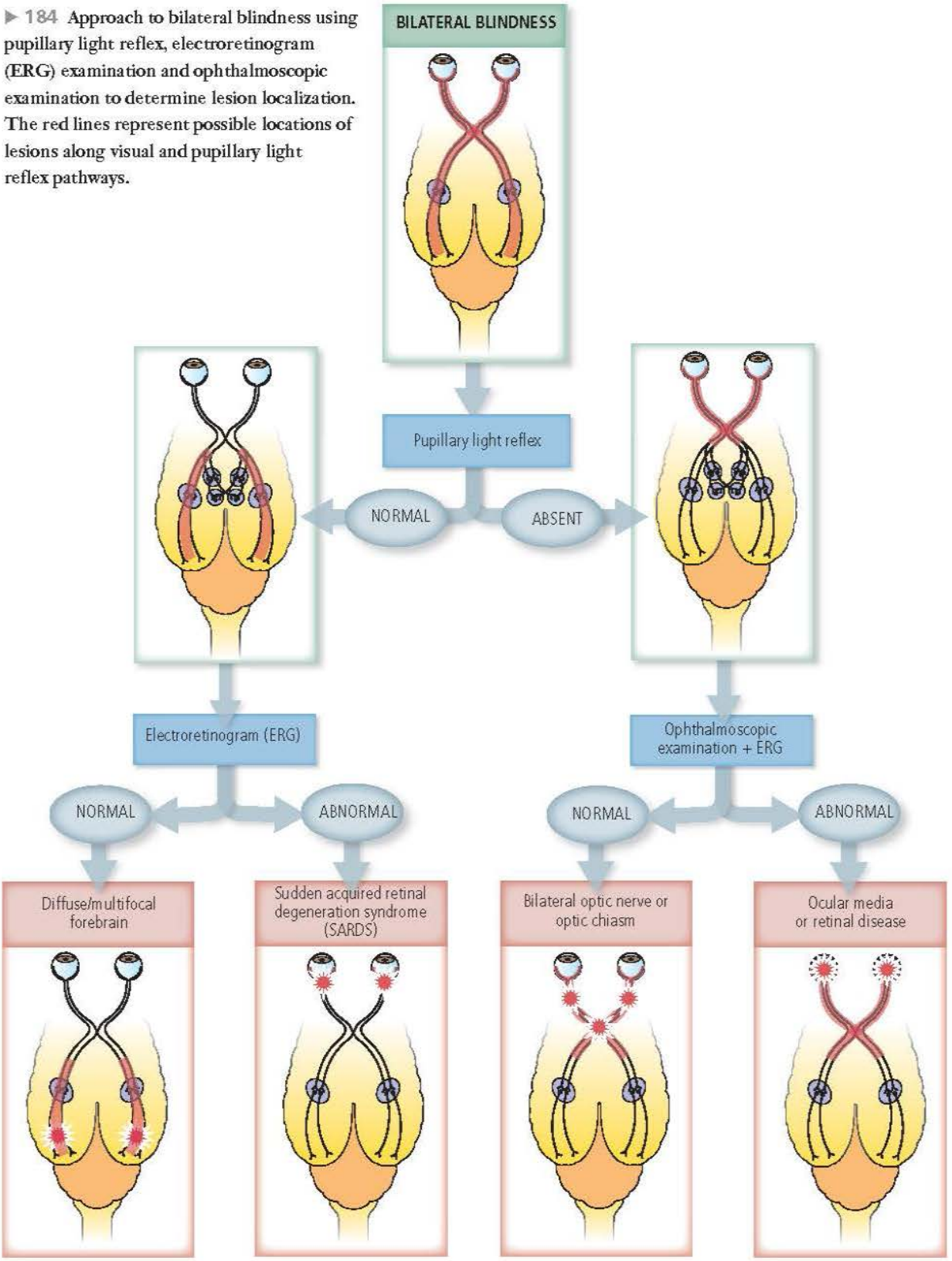
- **Conscious vision** can be tested by having the patient negotiate an obstacle course, or track objects and/or by utilizing the visual placing responses (see Chapter 1 for details of these tests). Conscious vision requires intact peripheral and central visual pathways (see **179, 182, 183**).
- The **dazzle reflex** (squint reflex) is evaluated by directing an extremely bright light source towards the retina. This reflex involves optic tract axons that synapse in the midbrain and subsequently project onto the facial nucleus, eliciting eyelid closure. This reflex pathway does not involve the cerebrum.
- **Mentation or behaviour, response to nasal stimulation and postural reactions** should be evaluated in all patients with visual loss. If abnormal, these may help localize the lesion to the central visual pathways. However, normal mentation, behaviour, nasal sensation and postural reactions do not exclude a central lesion.

Systematic approach to the blind animal

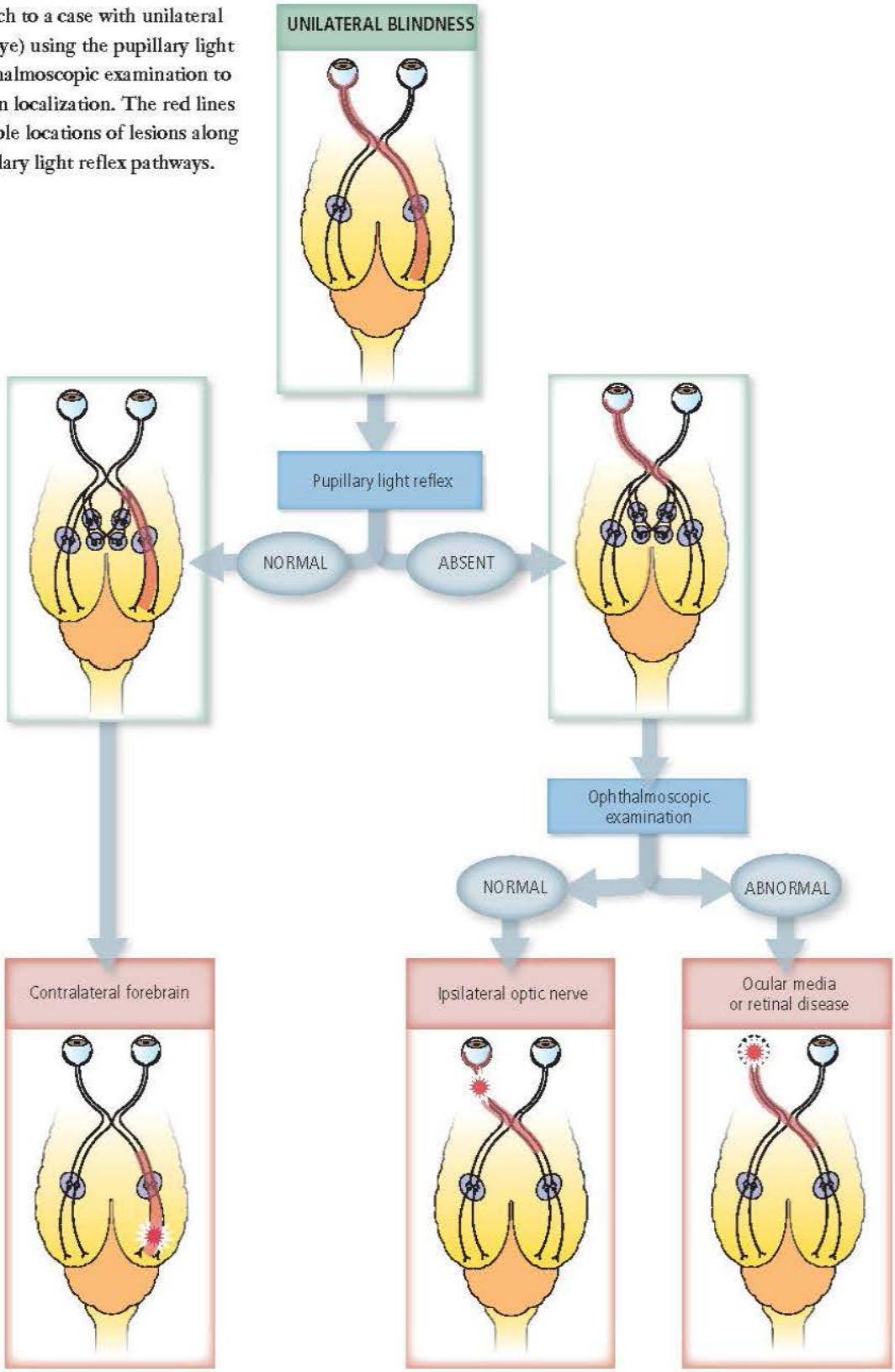
Step 1. Is the animal unilaterally or bilaterally blind?

This question is primarily answered by evaluating the menace response in each eye separately. If the menace is absent or delayed, the eyelids must be assessed for their ability to close by eliciting the palpebral reflex. If facial paralysis is present, eyeball retraction, elevation of the third eyelid and head retraction may help in the assessment of vision. If facial paralysis is present or if there is doubt about the result of the menace response testing, the patient's ability to navigate an obstacle course and/or the visual placing response should be evaluated (if the animal's size allows it to be lifted) (**184, 185**, pages 234 and 235).

▶ 184 **Approach to bilateral blindness using pupillary light reflex, electroretinogram (ERG) examination and ophthalmoscopic examination to determine lesion localization. The red lines represent possible locations of lesions along visual and pupillary light reflex pathways.**



▶ 185 Approach to a case with unilateral blindness (left eye) using the pupillary light reflex and ophthalmoscopic examination to determine lesion localization. The red lines represent possible locations of lesions along visual and pupillary light reflex pathways.



Step 2. Is the blindness peripheral or central?

Following the menace response, the clinician should evaluate the pupil size and PLRs to determine if the lesion is affecting portions of the peripheral or central visual pathways (see **182–185**). With a lesion of the peripheral visual pathways the PLR is expected to be absent, while it is intact with lesions of the central visual pathways. It should be noted that the PLR requires fewer intact axons than conscious perception of vision and, therefore, partial lesions of the peripheral visual pathways may cause loss of vision while sparing the PLR, creating the illusion of a lesion affecting the central visual pathways. In general, central blindness may be accompanied by other forebrain signs such as abnormal behaviour, seizures, sensory (facial/nasal hypalgesia) deficits and postural reaction deficits. These sensory and postural reaction deficits, as for the visual deficits, are all contralateral to the side of the forebrain lesion. Therefore, careful attention should be given to CN function, mentation and postural reaction evaluation (see Chapter 1).

The pupils should be assessed for symmetry in ambient light and in a dark room. A bright light source should then be directed into each eye individually; normal patients have rapid constriction of the pupil into which the light is directed (direct PLR) and the opposite pupil also should constrict (indirect or consensual PLR). In addition to optic and oculomotor nerve lesions, there are several possible localizations for PLR deficits. If a direct PLR is not elicited in one eye, the clinician should direct the light as close to that eye as possible and direct it around all aspects of the ocular fundus. If there is still no response present, the clinician should swing the light to the other eye and the non-responsive pupil should be assessed for constriction. If the non-responsive pupil is the result of an ocular or optic nerve lesion, it will constrict when the light is directed into the contralateral eye (i.e. positive indirect PLR). Such testing may need to be repeated multiple times to differentiate between a retinal/optic and oculomotor nerve problem.

Step 3. Is the lesion focal, multifocal or diffuse within the visual pathways?

See *Table 59*.

Table 59 **Lesion localization within the conscious visual pathway**

UNILATERAL OR BILATERAL BLINDNESS?	INTACT PLR?	PERIPHERAL OR CENTRAL BLINDNESS?	LESION DISTRIBUTION
Unilateral	No	Peripheral	Focal lesion of the ocular media, retina or optic nerve
	Yes	Central	Focal lesion in the contralateral distal part of the optic tract, lateral geniculate nucleus, optic radiation or visual cortex (i.e. contralateral forebrain)
Bilateral	No	Peripheral	Multifocal lesion of the ocular media, retina, optic nerves or focal lesion of the optic chiasm
	Yes	Central	Multifocal or diffuse lesion in the optic tracts, lateral geniculate nuclei, optic radiations or visual cortices (i.e. bilateral forebrain)

DIFFERENTIAL DIAGNOSIS

Conditions to be considered when evaluating a dog or cat presented with acute blindness are listed in *Tables 60* and *61*.

DIAGNOSTIC APPROACH

The diagnostic approach taken for the patient with acute visual loss depends on the neuroanatomical diagnosis (see **184, 185**). If the neuroanatomical diagnosis is unclear, the patient should be evaluated for both peripheral and central blindness.

Peripheral blindness

- Ophthalmic examination to check for lens luxation, hyphaema, glaucoma, uveitis, retinal detachment, chorioretinitis and papilloedema.
- Imaging of the lens and retina with ultrasound if direct visualization is not possible due to turbidity of the ocular media or cataract.
- Electroretinogram (ERG) detects retinal response to various intensities and frequencies of light. This is the diagnostic of choice in suspected cases of SARDS.
- Imaging of the optic nerves with CT or MRI for optic neuritis and optic nerve tumours.
- CSF analysis may disclose a mononuclear pleocytosis in cases of optic neuritis.
- Serology and PCR on serum and/or CSF for regional infectious diseases.

Central blindness

- Metabolic profile (CBC, serum biochemistry, bile acid stimulation test, urinalysis) if neurological examination suggests diffuse forebrain anatomical diagnosis.
- Advanced brain imaging (CT or MRI).
- CSF analysis.
- Serology and PCR on serum and/or CSF for regional infectious diseases.

Table 60 **Causes of unilateral acute blindness**

DISEASE MECHANISM	PERIPHERAL BLINDNESS	CENTRAL BLINDNESS
Vascular		Brain infarct* Brain haemorrhage
Inflammatory	Retinitis/chorioretinitis Retrobulbar abscess/cellulitis Infectious or non-infectious optic neuritis	Infectious encephalitis (viral, protozoal, fungal, bacterial, rickettsial)* Meningoencephalitis of unknown aetiology (GME, necrotizing, idiopathic)*
Traumatic	Trauma to the globe and orbit*	Head trauma*
Anomalous	Hyphaema, anterior uveitis, glaucoma, lens luxation, corneal oedema	Intracranial intra-arachnoid cyst Porencephaly/hydranencephaly
Neoplastic	Neoplasia of the optic nerve or neoplasia compressing the optic nerve* Ocular lymphoma	Primary or secondary brain tumour*

* Common cause

Table 61 **Causes of bilateral acute blindness**

DISEASE MECHANISM	PERIPHERAL BLINDNESS	CENTRAL BLINDNESS
Vascular	Retinal detachment and/or haemorrhage secondary to arterial hypertension*	Brain haemorrhage
Inflammatory/infectious	Retinitis/chorioretinitis Infectious or non-infectious optic neuritis*	Infectious encephalitis (viral, protozoal, fungal, bacterial, rickettsial)* Meningoencephalitis of unknown aetiology (GME, necrotizing, idiopathic)*
Traumatic	Trauma to the globes and orbits	Head trauma*
Toxic	Enrofloxacin toxicity (cats) Ivermectin toxicity (dogs)	Lead poisoning
Anomalous	Hyphaema, anterior uveitis, glaucoma, lens luxation	Intracranial intra-arachnoid cyst Porencephaly/hydranencephaly Hydrocephalus
Metabolic		Hypoxia/ischaemia/excitotoxicity (e.g. post ictal) Hepatic encephalopathy* Osmotic abnormalities (Na^+ imbalance) Hypoglycaemia* Ketoacidosis*
Neoplastic	Tumour of the optic chiasm or in the vicinity of the optic chiasm (meningioma, pituitary macroadenoma)	Primary or secondary brain tumour*
Degenerative	Sudden acquired retinal degeneration syndrome (SARDS)*	

* Common cause

COMMON CAUSES OF PERIPHERAL BLINDNESS

See *Tables 60* and *61*

Sudden acquired retinal degeneration syndrome

Overview

SARDS is an acute, progressive retinal disorder resulting in bilateral visual deficits to complete vision loss occurring over days to weeks; occurs in middle aged to older dogs (≥8 years of age). The aetiology is unknown, but several theories exist. Dachshunds, Miniature Schnauzers, Beagles and Brittanys are overrepresented. There is an initial apoptosis of the photoreceptor layer in the retina n the acute stages; retinal atrophy is seen in later stages. Some dogs with SARDS have been reported as having autoantibodies against neuron-specific enolase (NSE), although it is unclear whether these play a causative role in SARDS or whether they are the result of retinal destruction by another mechanism.

Clinical presentation

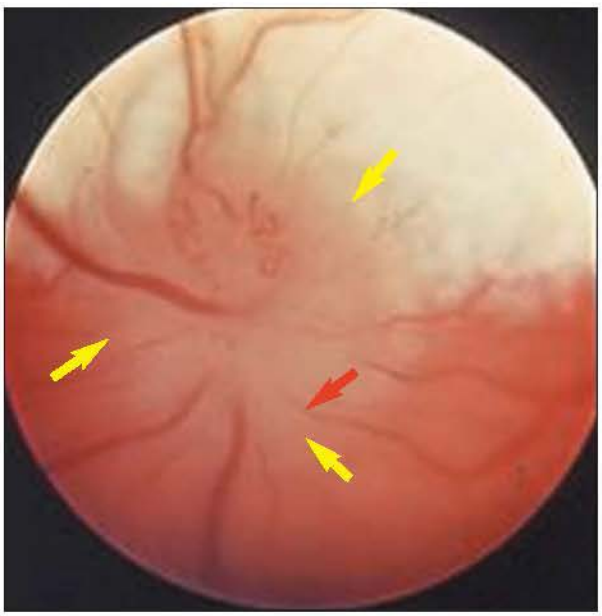
Ocular examination commonly reveals conjunctival hyperaemia, bilateral mydriasis and decreased to absent PLRs bilaterally. *Note:* PLR can initially be normal, creating the illusion of a more central lesion. A fundic examination may be normal in the early stages; a hyperreflective fundus and vascular attenuation can be seen in the later stages.

Diagnosis

ERG is required to distinguish SARDS from other lesions responsible for acute blindness. Dogs diagnosed with SARDS are commonly presented with concurrent clinical, physical and historical findings consistent with hyperadrenocorticism at the time of vision loss, but any association between the diseases is unknown at this time. Routine ACTH stimulation testing to evaluate cortisol and sex hormones, BP screening and urinalysis for protein/creatinine ratio are recommended in these animals.

Management

There is no treatment. The prognosis is grave for return of vision. Cushing's-like signs usually resolve within months.



▲ 186 Photograph of the fundus of a dog with optic nerve oedema. Note the blurred edges of the optic disc (yellow arrows) and changes in the calibre of superficial vessels (red arrow).

Papilloedema

Overview

Papilloedema is a process secondary to increased ICP or compression of optic nerve fibres causing 'back up' of CSF surrounding optic nerve fibres and secondary oedema of the optic disc. It can also be seen with conditions causing widespread myelin oedema (e.g. some metabolic or toxic disorders such as hexachlorophene poisoning) and orbital space-occupying lesions. Papilloedema needs to be differentiated from hypermyelination of the optic disc (pseudopapilloedema). Increased ICP can be due to trauma, a cerebrovascular accident (CVA) (see Chapter 17), meningoencephalitis or, most commonly, an intracranial tumour (meningioma, glioma, pituitary macroadenoma, metastatic brain tumour).

Clinical presentation

A fundic examination reveals loss of visualization of optic disc margins and changes in the calibre of superficial retinal blood vessels; neurological deficits will reflect the location of the lesion (**186**).

Diagnosis

Diagnosis is made by determining the underlying cause:

- Advanced brain imaging for CVAs and malformations.
- Advanced brain imaging +/- CSF analysis/biopsy for brain tumours and meningoencephalitis.

Management

Treatment of the underlying cause is essential. For increased ICP, mannitol (0.5–2.0 g/kg IV) can be given over 15 minutes and repeated in 30 minutes. Furosemide (0.5–1.0 mg/kg IV) can be given following mannitol administration. For increased ICP in a normotensive animal, 1–2 ml/kg of 7% hypertonic saline can be given IV over 5–10 minutes and repeated if needed. For increased ICP in a hypotensive animal, 4 ml/kg 7% hypertonic saline can be given IV over 5–10 minutes.

Corticosteroids (dexamethasone, 0.05–0.1 mg/kg IV q24h; prednisone, 0.5–1 mg/kg PO q24h) can be administered to decrease peri-tumoural oedema if present.

The prognosis is dependent on the aetiology.

Optic neuritis

Overview

Optic nerves are covered by meninges and may be affected by similar disease processes that affect the CNS. Optic neuritis is an acute, progressive inflammation of the optic nerves. There are several causes of optic neuritis including ocular GME, meningoencephalitis of unknown aetiology (MUA) and infectious disease (viral, rickettsial, fungal). (See Chapter 19 for further details on these diseases.)

Clinical presentation

Bilateral blindness is often seen. A fundic examination reveals loss of visualization of optic disc margins, dilatation of retinal veins and elevation of optic disc(s) and/or haemorrhage and/or tapetal reflective changes (**187**).

Diagnosis

Diagnosis is made by advanced brain imaging (CT, MRI), CSF analysis, titres and PCR. Biopsy is rarely performed in an antemortem setting.



▲ **187** **Photograph of the fundus of a dog with optic neuritis. Note the poor demarcation associated with the oedema and discoloration of the optic disc (arrows) caused by the inflammation of the optic nerve.**

Management

Treatment is dependent on the underlying cause:

- GME or MUA. Corticosteroids (2–4 mg/kg PO q24h tapered over 4 months until 0.5 mg/kg q48h depending on neurological signs); may need second immunosuppressive agent (e.g. cytosine arabinoside, cyclosporine). (See Chapter 19.)
- Antibiotic therapy for 4–6 weeks if there is an infectious aetiology. (See Chapter 19.)

The prognosis for return of vision is guarded to poor for infectious causes; the prognosis is fair for GME, but relapses and permanent vision loss may occur.

Retrobulbar abscess

Overview

A retrobulbar abscess is on occasion an acute, progressive condition causing unilateral visual deficits to complete blindness. The abscess can be due to a penetrating foreign body caudal to the last upper molar tooth, usually through the oropharyngeal region.

Clinical presentation

Physical examination reveals fever and exophthalmos due to a firm, painful mass in the retrobulbar space. Dysphagia and/or pain when opening the mouth may be present. Ocular examination reveals unilateral visual deficits and a diminished ipsilateral PLR and menace response, conjunctival hyperaemia, decreased retropulsion of the globe and third eyelid protrusion.

Diagnosis

Diagnosis is based on leukocytosis with neutrophilia, advanced imaging (CT, MRI), ultrasound and fine-needle aspiration with cytology and microbiological culture.

Management

The abscess should be drained through the oral cavity. Anti-inflammatories and broad-spectrum antibiotics (e.g. amoxicillin and clavulanic acid, 15 mg/kg PO q12h for 4–6 weeks) should be given until bacterial culture and sensitivity results are available. Soft food should be fed for 3–4 days. The prognosis is guarded to good for return of vision.

Optic nerve tumours

Overview

Optic nerve tumours can present as acute, progressive, unilateral visual loss. They most commonly occur in geriatric patients (≥9 years old), but can occur in younger patients. Meningioma is the most common tumour affecting the optic nerve, followed by gliomas; lymphoma and metastatic haemangiosarcoma have been reported.

Clinical presentation

Clinical signs include unilateral vision loss, which can progress to bilateral vision loss. Physical examination findings reveal a retrobulbar mass with exophthalmos (more commonly with meningiomas), retinal haemorrhage (more commonly with gliomas), secondary papilloedema, absent PLR and menace response ipsilateral to the lesion, and retinal detachment (more commonly with gliomas).

Diagnosis

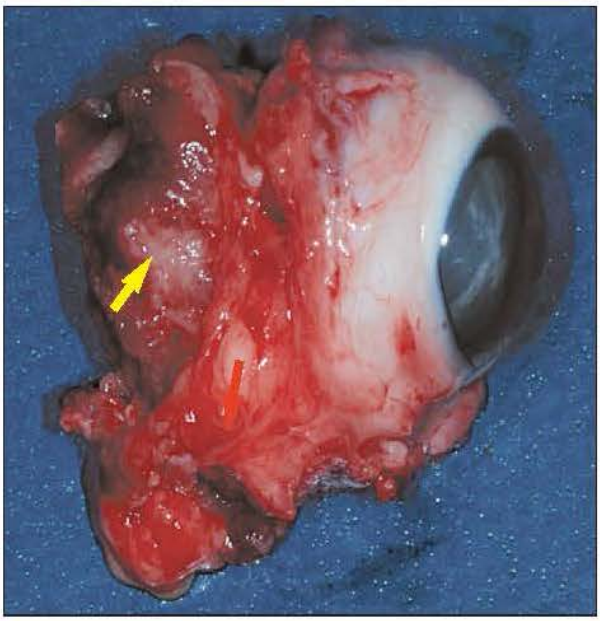
Diagnosis is made by advanced imaging (CT, MRI) (**188**) +/- CSF analysis. A definitive diagnosis is made by biopsy and histopathology of the affected optic nerve at the time of enucleation (**189**).

Management

If the tumour is close to the retrobulbar space, enucleation with surgical excision of the affected portion of the optic nerve can result in a cure. The prognosis is guarded to poor if the tumour is not completely excised, as recurrence and progression are likely to occur.



▲ 188 T2-weighted MR image in the dorsal plane of an optic nerve meningioma (arrow). Note the enlarged optic nerve as compared with the normal side.



▲ 189 Gross image of an eye with an optic nerve meningioma (arrow) severed from its attachment to the optic chiasm.

ACUTE TREMORS AND INVOLUNTARY MOVEMENTS

Marc Kent

INTRODUCTION

Involuntary muscle movements refer to a group of clinical syndromes in which sustained or episodic muscle contractions occur involuntarily in the conscious animal. In veterinary medicine the subject of involuntary muscle movements has received little attention. This may reflect their relatively infrequent occurrence in practice. Compounding this lack of study is a lack of standard, well-accepted terminology to describe the various syndromes of involuntary muscle movements. Not only does this make classification arduous, but it also creates difficulty in comparing various clinical manifestations. This chapter is founded on a proposed classification scheme derived from appropriate medical definitions.

Involuntary muscle movements may originate from a disturbance in either the muscle or the LMN.

- Disturbance of muscle. When originating from muscle, altered muscle membrane excitability results in sustained muscle contraction called **myotonia**. Myotonia can be congenital or acquired. For example, congential myotonia has been reported in the Miniature Schnauzer. Acquired myotonia can occur secondary to hyperadrenocorticism.
- Disturbance of the LMN. When originating as a result of spontaneous discharges of the LMN, the following terms are applied: tetanus, tetany, myoclonus, myokymia and movement disorder:
  - **Tetanus** is defined as constant contraction of the extensor muscles and is discussed in detail in Chapter 25. The most common cause of tetanus occurs secondary to the toxin produced by *Clostridium tetani*.
  - **Tetany** is defined as variably intermittent contractions of the extensor muscles. The most well-known syndrome example of tetany occurs secondary to hypocalcaemia.
  - **Myoclonus** is the sudden contraction followed immediately by relaxation of a specific muscle group. One of the most common syndromes associated with myoclonus occurs secondary to infection with canine distemper virus. With rapid and repeated cycles, repetitive myoclonus manifests as a **tremor**.
  - **Myokymia**. Simultaneous or sequential spontaneous contractions caused by depolarization of multiple motor units manifesting as a rippling of the muscle.
  - **Movement disorders** are sudden, involuntary contractions of specific muscle groups that may persist over a period of time either at rest or during activity in an awake, conscious animal.

A selection of involuntary muscle movements that may be encountered in small animal emergency practice are described in this chapter; these include constant repetitive myoclonus, idiopathic generalized tremor syndrome, intermittent head bobbing and myokymia, as well as breed-specific movement disorders.

NEUROANATOMICAL BASIS

The neuroanatomical basis for most of these involuntary muscle movements is unknown. In most instances these conditions are rarely life threatening or incapacitating to the affected animal, therefore large-scale studies with thorough histological evaluation of the nervous systems of affected animals have not been performed. Where investigations have been done, a functional disorder, probably involving abnormal neurotransmitters or their receptors, has been speculated.

NEUROLOGICAL EVALUATION

Many involuntary muscle movement disorders are episodic in nature. Consequently, at the time of presentation neurological evaluation may be normal. Even in animals with constant involuntary muscle movements, a neurological examination may reveal few deficits. Therefore, a thorough anamnesis is crucial in the evaluation of affected animals. Paramount to establishing the existence of an involuntary muscle movement is ensuring that the affected animal maintains a normal mental state (normal consciousness) during the episode. Descriptions of the involuntary muscle movement should include whether it was limited to an isolated anatomical area, such as a single limb or the head (focal), or involved the body and all the limbs (generalized). Knowing whether the movement persists during relaxation or sleep is also helpful. Questioning owners about a possible trigger for the movement can also provide important information. When possible, owners should be asked to provide a video recording of an episode to assist the clinician with the evaluation of the affected animal.

When signs are present, affected animals often display tremors that vary in amplitude (fine to coarse) and frequency (slow to rapid). Tremors may wax and wane with excitement and relaxation. Movements may affect isolated areas (focal) or involve the body and limbs (generalized). Along with tremors, increased extensor tone is often present in generalized disorders. In some disorders, hypertonicity is the predominant or sole manifestation. Gait analysis may be difficult to evaluate in animals with generalized tremors and increased extensor tone. Despite this, weakness and ataxia are largely absent. However, affected animals can be incapacitated by an inability to move their limbs because of sustained contraction of extensor or flexor muscle groups. Postural reactions and spinal and CN reflexes are generally normal. As a result of a lack of definitive deficits, defining a neuroanatomical diagnosis is difficult.

DIFFERENTIAL DIAGNOSIS

Creating a differential diagnosis list for many involuntary muscle movement disorders is challenging. Given their episodic nature in many instances, clinicians are often faced with providing an assessment, diagnosis, treatment plan and prognosis based solely on a description of the event provided by the owner. Moreover, some involuntary muscle movement disorders are diagnosed based on pattern recognition (i.e. diagnosed simply from observation and the knowledge of a disorder in a specific breed with a unique characteristic presentation). In a few disorders a more typical orderly differential diagnosis list and diagnostic plan can be made. In the end, an accurate and thorough description, combined with a systematic classification of involuntary muscle movement disorders, is essential in establishing a diagnosis.

Consideration of the differential diagnoses and their typical characteristics can assist with their investigation and differentiation. Some of these differentials have specific clinical characteristics rather than diagnostic test results, and these are outlined below.

- **Focal seizures.** The most important differential diagnosis for involuntary muscle movement disorders is simple, focal seizures. Focal seizures are recognized in animals with stereotypic, episodic muscle movements. As such, focal seizures can be easily misconstrued as an involuntary muscle movement. Given the difficulty in the clinical differentiation from simple focal seizures, along with a lack of a defined diagnostic algorithm for involuntary muscle movement, diagnostic testing should be aimed at eliminating structural disease of the CNS from consideration. Consequently, performing an MRI scan of the brain, along with CSF analysis, is recommended. In some cases, implementing a therapeutic trial of anticonvulsants may be appropriate (see Chapter 7).
- **Sleep disorders.** Animals may have abnormally excessive movements during sleep. Such movements may be limited to the limbs and appear as if the animal is trying to run. Additionally, more complex behaviour, such as barking, crying, growling and biting, sometimes along with the animal standing up, can occur during REM sleep.

These movements can be differentiated from involuntary muscle movements, as animals with excessive movements during sleep have cessation of the activity when woken.

- **Intention tremors.** Another important differential diagnosis for involuntary muscle movement disorders is intention tremors resulting from cerebellar disease. Intention tremors due to diffuse/multifocal lesions involving the cerebellum occur only with voluntary movements and are absent at rest. They are most evident in the head movement observed when the animal is eating or drinking. They appear as gross, jerky movements of varying amplitude. Importantly, animals with cerebellar disease display a cerebellar ataxia described as a dysmetria (most evident as hypermetria), a truncal sway and a broad-based posture when standing. Postural reactions, such as hopping, may be slightly delayed and display a 'burst-like' quality as the animal tends to slap the foot to the ground; signs are not intermittent.

Table 62 **Differential diagnoses for generalized tremor syndromes**

DISEASE MECHANISM	EXAMPLES
Vascular	
Inflammatory/ infectious	Infectious and sterile meningoencephalitis*
Toxic	Pyrethrins*, organophosphate*, metaldehyde*, mycotoxin*, drug induced
Anomalous	Congenital hypomyelinogenesis
Metabolic	Electrolyte imbalance (calcium, magnesium)*, hypoglycaemia*, hypothermia*, hyperthyroidism*
Idiopathic	Idiopathic generalized tremors*
Degenerative	Lysosomal storage disease, cerebellar abiotrophy, peripheral nerve diseases (including benign postural tremors of older dogs)

* Common cause

Head bobbing and idiopathic generalized tremors are most frequently misinterpreted as a cerebellar disorder. With head bobbing, the gait is normal and the movement can be interrupted with voluntary changes in head and neck posture. In general, ataxia is minimal or absent with idiopathic generalized tremors. Additionally, tremors tend to be fine and do not increase in amplitude or rate with voluntary movement.

Differential diagnoses for generalized tremor syndromes are presented in *Table 62*.

DIAGNOSTIC APPROACH

The diagnostic plan will vary depending on the clinical presentation of the affected animal. Often, the aim of the plan is to eliminate from consideration other disease processes that could mimic similar clinical signs (**190**, next page).

Idiopathic generalized tremors

- CBC, biochemical evaluation and urinalysis to exclude underlying metabolic (especially fasting glucose and electrolytes), endocrine or toxicological causes of generalized tremors.
- Toxicological screening may be pursued based on clinical suspicion and supportive history.
- MRI of the brain.
- CSF analysis.

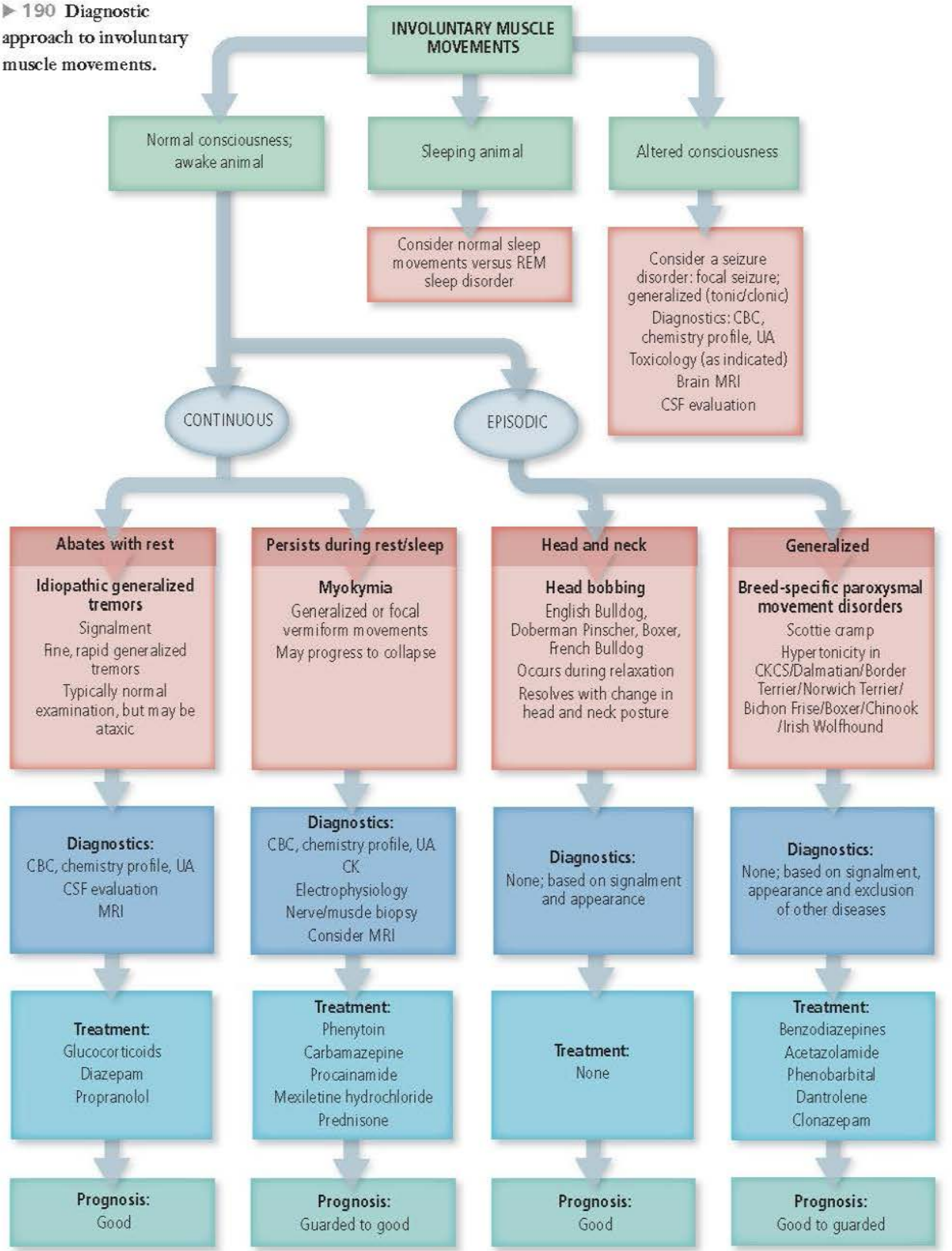
Head bobbing

- If classical movement is observed in the typically affected breed of dog, diagnostic testing is not performed unless the dog is showing other neurological signs.
- Similar presentations have been seen due to focal thalamic lesions, suggesting an MRI could be useful.

Myokymia

- CBC, biochemical evaluation and urinalysis to exclude underlying metabolic or endocrine disorders that could affect peripheral nerves or muscles.
- CK activity.

▶ 190 **Diagnostic approach to involuntary muscle movements.**



- Electrophysiology (EMG and motor nerve stimulation studies).
- Consider MRI of the brain (if myokymia is limited to the face) or spinal cord (if myokymia observed in the limbs).
- Consider muscle and motor nerve fascicular biopsies.

Movement disorders

- CBC, biochemical evaluation and urinalysis to exclude underlying metabolic (including organic acidurias) or endocrine disorders.
- Discontinue any drugs associated with movement disorders.
- Consider therapeutic trial of oral diazepam, clonazepam, acetazolamide or dantrolene in animals with dystonia.
- In an attempt to exclude simple focal seizures related to structural disease of the brain, consideration should be given to the following options:
  - MRI of the brain.
  - CSF analysis.
  - EEG.
  - Serum and CSF serology, PCR testing or microbiology where indicated.
  - Consider therapeutic trial of anticonvulsants, especially levetiracetam and zonisamide.

COMMON CAUSES OF ACUTE TREMORS AND INVOLUNTARY MOVEMENTS

The emergency treatment of a general acute tremor case is outlined in **191** (next page). More specific condition treatments are detailed below and in **190**.

Idiopathic generalized tremor syndrome

Overview

Idiopathic generalized tremor syndrome is an acquired, action-related repetitive myoclonus in dogs. It is also known as 'little white shaker disease'. The most common breeds affected are the West Highland White Terrier, Cocker Spaniel and Maltese. The condition typically affects dogs between 1 and 5 years of age, weighing <15 kg and with a white coat, but it can affect any breed regardless of age, size and coat colour.

The syndrome is occasionally associated with vestibulocerebellar signs such as head tilt and abnormal nystagmus or tremor of the eyeball (opsoclonus).

Clinical presentation

There is acute onset of clinical signs – generalized rapid, fine tremors of the head and body – which may be progressive over several days. The condition worsens with excitement, reduces with relaxation and is absent during sleep. Rarely, cases have an associated absent menace response, inability to walk, weakness and seizures.

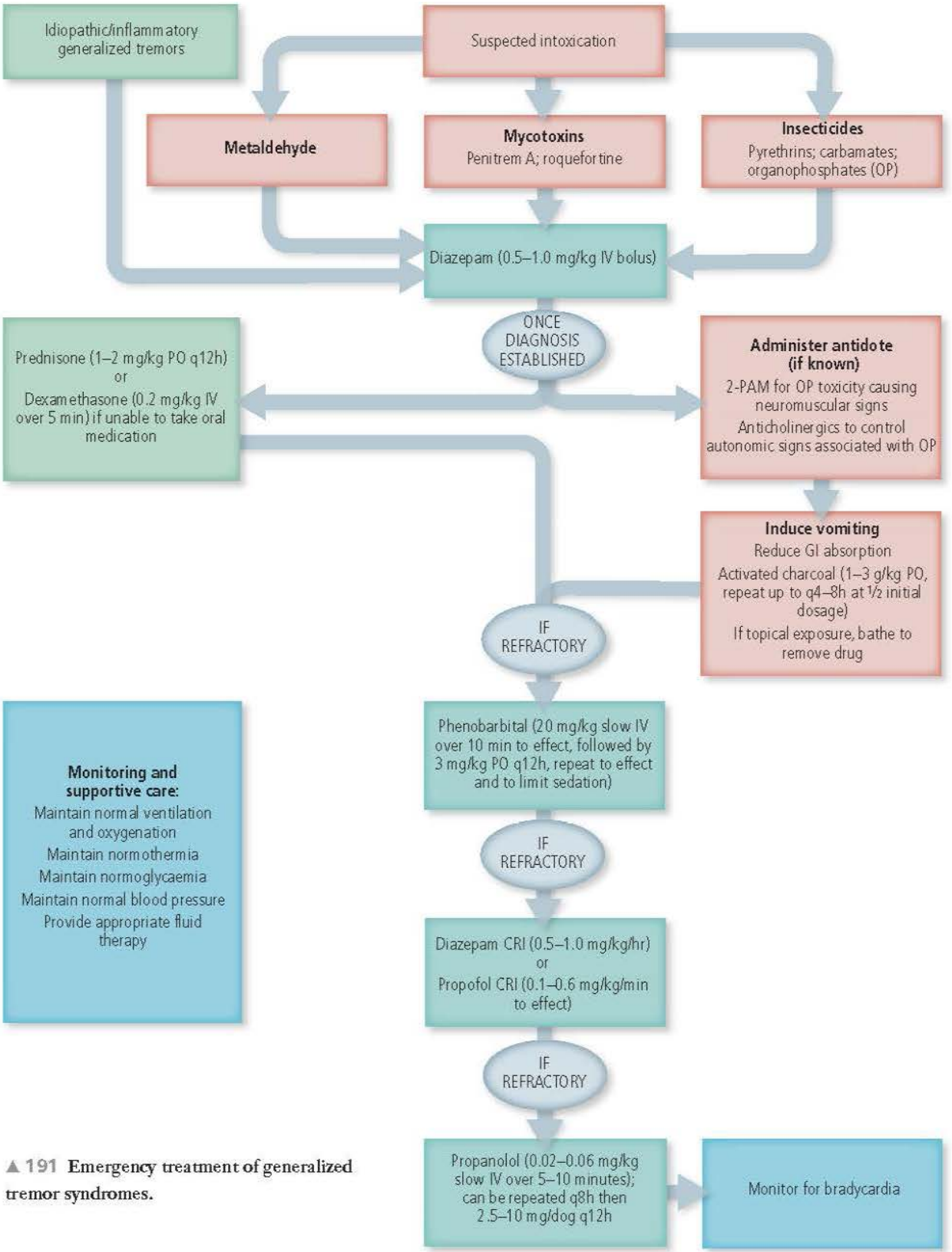
Differential diagnoses include disorders of myelination, CNS disease (degenerative), toxicity (pyrethrin/organophosphate, lead, metaldehyde, mycotoxins), physiological tremors (fear, pain, hypothermia), hypoglycaemia, hypocalcaemia and drug-induced dyskinesia (abnormal movement).

Diagnosis

Diagnosis is based on clinical suspicion after considering signalment, exclusion of similarly appearing disorders, MRI of the brain and CSF analysis.

Management

Treatment consists of immunosuppressive therapy with glucocorticoids (1–2 mg/kg PO q12h, then tapered over several months). Affected dogs usually respond to therapy in 2–3 days, but it may take up to 10 days to see an effect. Dogs not responding to glucocorticoids may require additional medications:



▲ 191 **Emergency treatment of generalized tremor syndromes.**

- Diazepam (0.5–1.0 mg/kg PO or IV q8h).
- Propranolol (dog: 2.5–10.0 mg/dog PO q8–12h).

The prognosis is excellent, with most dogs returning to normal. Recurrence is possible if the glucocorticoids are tapered too rapidly.

Head bobbing

Overview

Head bobbing is a postural, repetitive myoclonus syndrome involving the head and neck, characterized by acute onset with variable frequency of occurrence. The most common breeds affected are the English Bulldog and Doberman Pinscher. Other breeds include the Boxer, French Bulldog and mixed-breed dogs. Head bobbing typically affects dogs between 1 and 5 years of age. The pathophysiology is unknown, but it appears to be related to positioning of the head and neck, which suggests a defect in the stretch reflex of the intrafusal muscle spindle.

Clinical presentation

Episodes can last minutes to hours. Rapid coarse tremors of the head and neck are directed horizontally or vertically as if shaking the head and neck to say 'yes' or 'no', respectively. Head bobbing often occurs hours after heavy exercise while the animal is quiet and relaxed. Mentation and awareness are normal and the dog is able to walk and function normally during an episode.

Diagnosis

Diagnosis is based on observation of typical clinical signs in commonly affected breeds.

Management

During episodes, movement can be stopped when the dog rests its head on a surface, thereby not using the neck muscles to support the head. Movements can also be stopped by getting the dog to alter its head and neck position by offering a treat or calling the dog's attention.

There is no known treatment. The prognosis is excellent for this syndrome, as discernible structural lesions are absent and affected dogs are not bothered by the movement.

Myokymia

Overview

Myokymia is an episodic, non-postural repetitive myoclonus that can involve any muscle group(s). A specific phenomenon, myokymia is the clinical observation of rhythmic, undulating, vermiform (worm-like) or wave-like movements of the skin overlying contracting muscle fibres. It affects both dogs and cats and there is an acute onset and a progressive course.

Myokymia is the clinical manifestation of motor axon or motor nerve terminal hyperexcitability (known as neuromyotonia). In humans, myokymia occurs secondary to Guillain–Barré syndrome, multiple sclerosis, radiation plexopathy, brainstem tumours, timber rattle snake envenomation and a variety of autoimmune diseases, in particular one directed against voltage-gated potassium channels. Underlying causes have not been identified in animals.

Myokymia may occur in isolated muscle groups (focal) or affect body and limbs (generalized) simultaneously. The most common focal presentation involves facial muscles controlled by CN VII (facial nerve); sometimes it also affects the muscles of mastication. When generalized, myokymia is also known as continuous muscle fibre activity. One suggestion is that the condition is related to peripheral nerve hyperexcitability syndrome in Jack Russell Terriers, with an underlying ion channel disorder as the cause.

Clinical presentation

In Jack Russell Terriers signs begin at a mean age of 8 months. Movements are continuous and, importantly, persist during sleep and general anaesthesia. Animals with generalized disease may develop hyperthermia, progressive stiffness, limb contractures and collapse. Jack Russell Terriers with this disease frequently present with concurrent signs of hereditary ataxia and neuromyotomia (generalized muscle stiffness).

Differential diagnoses include disorders that result in muscle fasciculations and tremors, such as those observed in toxicities (pyrethrin/organophosphate, lead, metaldehyde, mycotoxins), physiological tremors (fear, pain, hypothermia), hypoglycaemia, hypocalcaemia and drug-induced dyskinesia.

Diagnosis

Diagnosis is based on the characteristic appearance of the movement of the overlying skin. A definitive diagnosis is based on EMG identification of myokymic and neuromyotonic discharges:

- Myokymic discharges are short, rhythmic or semi-rhythmic bursts of doublet, triplet or multiplets of motor unit potentials (MUPs) occurring at an interburst frequency of 5–62 Hz and an intraburst frequency of 150–280 Hz.
- Neuromyotonic discharges are long bursts of MUPs occurring at rates of 150–300 Hz that wax and wane in amplitude.

Affected animals have an elevated serum CK activity.

Management

Treatment involves drugs that stabilize muscle membrane potentials:

- Phenytoin (dog: 15–30 mg/kg PO q8h; cat: 2–3 mg/kg PO q24h).
- Carbamazepine (dog: 4–8 mg/kg PO q8–12h; cat: 2–6 mg/kg PO q12–24h).
- Procainamide (dog: 6–8 mg/kg PO q6–8h).
- Mexiletine hydrochloride (dog: 4–8 mg/kg PO q8h).

Animals with focal syndromes may not require treatment unless the tremors are affecting the animal's quality of life. The prognosis is variable depending on severity of clinical signs and response to therapy. The prognosis for focal syndromes is good, while generalized syndromes may not respond to therapy.

BREED-SPECIFIC PAROXYSMAL MOVEMENT DISORDERS

Various terms have been used to describe clinical observations in affected animals:

- **Dyskinesia** is a general term to describe hyperkinetic movement disorders.
- **Dystonia** is an involuntary sustained contraction of a group of muscles producing abnormal posture.
- **Chorea** is an abrupt, unsustained contraction of different muscle groups.
- **Athetosis** is a prolonged contraction of the trunk muscles resulting in bending and writhing of the body.
- **Ballism** is an abrupt contraction of the limb muscles, which results in flailing movement of the limbs.

Movement disorders encompass a wide range of abnormal movements. In an affected animal, such movements may not be stereotypic, varying not only in duration and frequency, but also in affected muscle groups. The most common clinical presentation is dystonia involving the hindlimbs, which clinically appears as increased extensor tone of the limbs. While all four limbs may be affected, the hindlimbs are often affected to a greater degree than the forelimbs. Episodes are often triggered by excitement or exercise.

Functional deficiencies in neurotransmitters or their receptors are implicated in the pathogenesis of these disorders. Structural lesions are usually absent. Loss of consciousness and awareness is not a feature of these conditions, which may help to differentiate them from some epileptic seizure activities.

Breed-associated dystonia and chorea (primarily of the hindlimbs)

Scottie cramp

Overview

Scottie cramp is a syndrome observed in Scottish Terriers consisting of involuntary sustained muscle contractions primarily affecting the hindlimbs. Signs begin within the first 1–3 years of age. The disease has a presumed autosomal recessive inheritance pattern, with variable expression of the clinical signs.

A functional deficiency in serotonin modulation of motor neuron function has been postulated:

- Expression of the disease varies inversely with CNS serotonin levels (i.e. more severe signs with decreased CNS serotonin levels and less severe with increased serotonin levels).
- Drugs that decrease CNS serotonin result in increased clinical signs (e.g. methionine).

Clinical presentation

With excitement, the hindlimbs assume a hypertonic, extended position or they may occasionally display exaggerated flexion of the limbs. The forelimbs become abducted and develop increased extensor tone. Affected dogs progressively develop a stiff stilted gait over a few minutes. Severely affected dogs assume an arched posture over their back and may fall into lateral recumbency with their head and tail flexed.

Diagnosis

Diagnosis is based on signalment and characteristic clinical signs. Signs can be induced with exercise 2 hours after administering methysergide (0.3 mg/kg PO), a serotonin antagonist.

Management

Treatment is aimed at muscle relaxation or increasing serotonin levels. Treatment also reduces the severity and duration of clinical signs (e.g. diazepam, 0.5–1.0 mg/kg PO or IV; acepromazine, 0.075–0.1 mg/kg PO or IM).

Although not currently documented, serotonin reuptake inhibitors may be useful for the treatment of this condition. The prognosis is generally good; however, severely affected dogs may be incapacitated without treatment.

Hypertonicity in Cavalier King Charles Spaniels

Overview

Hypertonicity in Cavalier King Charles Spaniels is also known as episodic falling, deer stalking, collapsing Cavalier and tetany. Affected dogs range in age from 1–4 years old. Candidate gene analysis has recently identified a microdeletion affecting the brevican gene (*BCAN*), which encodes the brain-specific extracellular matrix proteoglycan brevican. This will allow the development of rapid genotyping tests for this condition.

A syndrome involving hypertonicity of the hindlimbs, similar to that observed in the Scottish Terrier and Cavalier King Charles Spaniel, has also been reported in the Dalmatian, Irish Wolfhound and Norwich Terrier.

Clinical presentation

The clinical signs are very similar to those seen in Scottish Terriers. Excitement and exercise are associated with the development of clinical signs.

Diagnosis

Diagnosis is based on signalment and characteristic clinical signs. A genetic test exists for Irish Wolfhounds.

Management

Treatment reduces the severity and duration of the clinical signs. Oral acetazolamide (4–8 mg/kg PO q8–12h) usually results in complete resolution of clinical signs. Clonazepam (0.5 mg/kg PO q8–12h) can be used as an add-on to acetazolamide in refractory cases, but its effects may not be lifelong, as functional tolerance tends to develop.

The prognosis is good, as affected dogs are generally not incapacitated.

Breed-associated movement disorders (with generalized signs)

Although the specific breeds described below have been reported to be affected with movement disorders, any breed could exhibit a similar abnormality. For instance, the editors have seen several Labrador Retrievers exhibiting clinical signs similar to the Chinooks described below.

Bichon Frise

Overview

A movement disorder has been observed in young Bichon Frise dogs. Episodes occur randomly and can be associated with excitement and activity or occur at rest. There are variable severity, duration and frequency. Consistent observations are:

- Unilateral facial dystonia resulting in a grimacing expression.
- Dystonia of a single limb appearing as sustained hyperflexion of the affected limb.

- Flexion of the thoracic vertebral column causing the dog to assume a kyphotic posture.
- Chorea-like movement of a limb consisting of rapid flexion and extension of the limb.

Boxer

Overview

A movement disorder has been observed in young Boxer puppies. Episodes may be induced with excitement or stimuli such as loud noise. Involuntary movements differ between episodes in a single pup as well as between pups. There are variable severity, duration and frequency. Both male and female pups are affected. A genetic basis is suspected.

Consistent observations are:

- Dystonia of the facial muscles resulting in a grimacing expression.
- Athetosis of the neck musculature resulting in torticollis.
- Chorea-like movements of the limbs consisting of holding an extended limb off the ground, banging it on the ground in rapid succession, or sustained hyperflexion of a limb.

Chinook

Overview

A disorder referred to as episodic dyskinesia has been observed in Chinook dogs. Episodes consist of an inability to stand or walk, head tremors and involuntary flexion of one or multiple limbs. Dogs maintain normal consciousness during the episode. Episodes last from seconds to hours. Affected dogs may also have generalized seizures, raising the possibility that this syndrome represents a seizure disorder rather than a movement disorder. An autosomal recessive pattern of inheritance is suspected.

Border Terrier

Overview

A syndrome known as canine epileptoid cramping syndrome (Spike's disease) has been observed in Border Terriers. Episodes consist of gait abnormalities ranging from ataxia to an inability to stand, contractions of abdominal and lumbar muscles and contractions of the appendicular muscle resulting in extensor rigidity or flexion of the limbs. Increased intestinal motility is suspected based on hearing borborygmus. Affected dogs may be in pain during the episode. A genetic basis for the syndrome is suspected. Hypoallergenic dietary therapy has been proposed by some breeders (http://www.borderterrier-cecs.com/index.htm).

Drug-induced movement disorders

Phenobarbital

Overview

Dyskinesia has been associated with phenobarbital administration. Clinical signs consist of whole body jerking movements, severe enough to cause the affected dog to fall, and intermittent fine tremors of the facial, neck and shoulder musculature. Agitation and restlessness have also been reported. Signs gradually diminish and resolve as phenobarbital is tapered and discontinued.

Propofol

Overview

A variety of abnormal movements can occur on recovery from propofol administration. Clinical signs consist of opsoclonus (rapid abnormal eye movements) and myoclonus. Clinical signs resolve with discontinuation of the drug.

HEAD TILT AND NYSTAGMUS

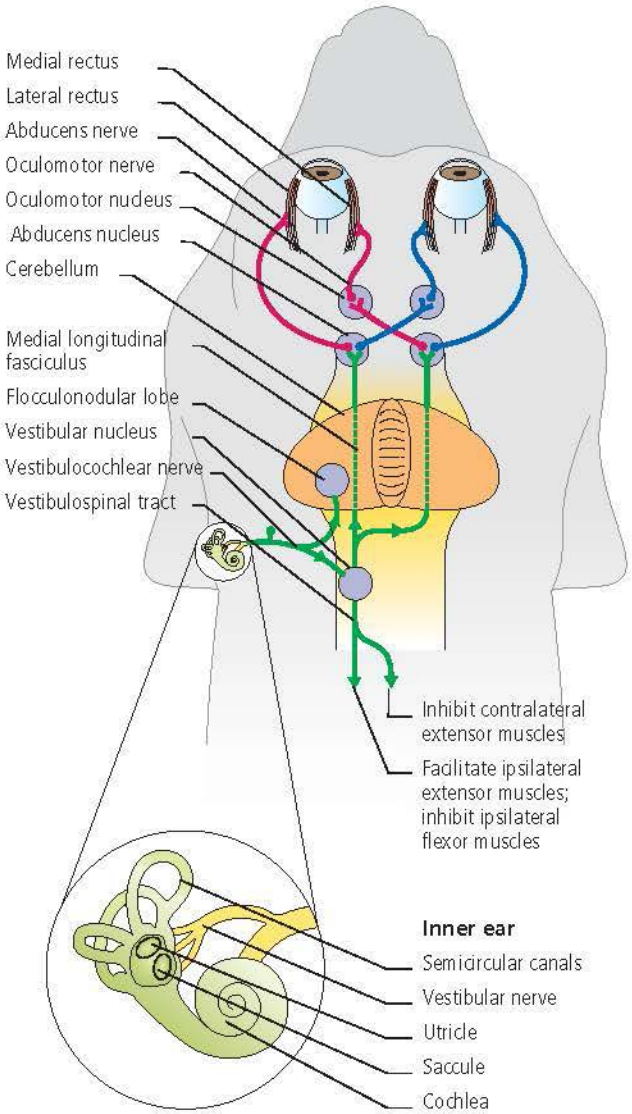
Laurent Garosi

INTRODUCTION

Head tilt and nystagmus are frequent clinical manifestations of a vestibular disorder, although a head tilt alone may be observed with otitis externa or other causes of aural irritation. The vestibular system is essential in maintaining balance and preventing the animal falling over by keeping and adapting the position of the eyes, head and body with respect to gravity. It is therefore not surprising that disease of the vestibular system results in some of the most dramatic and distressing neurological signs. In addition to head tilt and abnormal nystagmus, positional strabismus, falling, rolling, leaning, circling, and ataxia commonly result. Clinical signs of vestibular disease may be a result of lesions involving either the receptor organs in the inner ear or the vestibular portion of CN VIII (i.e. peripheral vestibular disease) or lesions involving the brainstem vestibular nuclei or vestibular centres in the cerebellum (i.e. central vestibular disease). If an animal is presented with a head tilt and nystagmus, a lesion must be localized to these particular sections of the vestibular apparatus before an appropriate differential diagnosis list can be established and further testing conducted.

NEUROANATOMICAL BASIS

The vestibular system is a sensory system. Its main function is to control balance and prevent the animal from falling over by maintaining and adapting the position of the eyes, head and body with respect to gravity. The vestibular system (**192**) consists of a receptor organ within the petrous temporal bone (inner ear), the vestibular nerve and a balance control centre at the back of the brain (four brainstem nuclei located in the rostral medulla oblongata on each side of the fourth ventricle).



▲ **192** **Schematic anatomy of the vestibular system.**



▲ 193 Head tilt in a cat with central vestibular syndrome.



▲ 194 Head and body turn (pleurothotonus) in a 10-year-old Boston Terrier with a right-sided forebrain tumour. Compared with a head tilt, the median plane of the head remains perpendicular to the ground, but the nose is turned to one side.

The receptor organ (macular receptors of the saccule and utricle located within the vestibule and crista ampullaris of the semi-circular duct located within the semi-circular canals) detects the position and movement of the head in space while the animal is standing at rest or when it is moving. The information on the position of the head is converted into electrical signals, which are sent via the vestibular nerve to the brain. The balance control centre in the brainstem processes this information and sends messages to the rest of the body to keep the animal upright (facilitatory effect on the ipsilateral extensor muscles of the limb via the vestibulospinal tract). Messages are also sent to the muscles controlling movement of the eyes (via medial longitudinal fasciculus and CNs III, IV and VI) to change the position of the eyes according to the position of the head. Finally, the brainstem vestibular nuclei receive some influence from higher vestibular centres in the thalamus and from vestibular centres in the cerebellum (flocculonodular lobe and fastigial nuclei). The latter have an inhibitory effect, mainly on the brainstem vestibular nuclei. Through these pathways, the vestibular system controls the position of the eyes, trunk and limbs based on the position and movement of the head.

Head tilt

Head tilt is described as a rotation of the median plane of the head along the axis of the body resulting in one ear being held lower than the other one (**193**). It occurs in vestibular disease as a result of the loss of anti-gravity muscle tone on one side of the neck. Head tilt must be differentiated from a head turn, where the median plane of the head remains perpendicular to the ground, but the nose is turned to one side (**194**). Such head turn is usually associated with a body turn (pleurothotonus) and circling. A head turn does not indicate a vestibular disorder and is usually towards the side of a forebrain lesion.

Nystagmus

Nystagmus is an involuntary rhythmic movement of the eyeballs. Physiological (or vestibular) nystagmus is a nystagmus that occurs in normal animals, while pathological nystagmus reflects an underlying vestibular disorder (**195**). In both instances the nystagmus has a slow and fast phase (i.e. jerk nystagmus). A physiological nystagmus can be induced in normal individuals by rotation of the head from side to side (oculovestibular reflex). It is best performed on a cat by holding the animal at arm's length and rotating it from side to side. It may only be seen at the end of the movement. This nystagmus stabilizes images on the retina during head movement. It is always observed in the plane of rotation of the head and consists of a slow phase in the direction opposite to that of the head rotation, with a fast phase in the same direction as the head rotation.

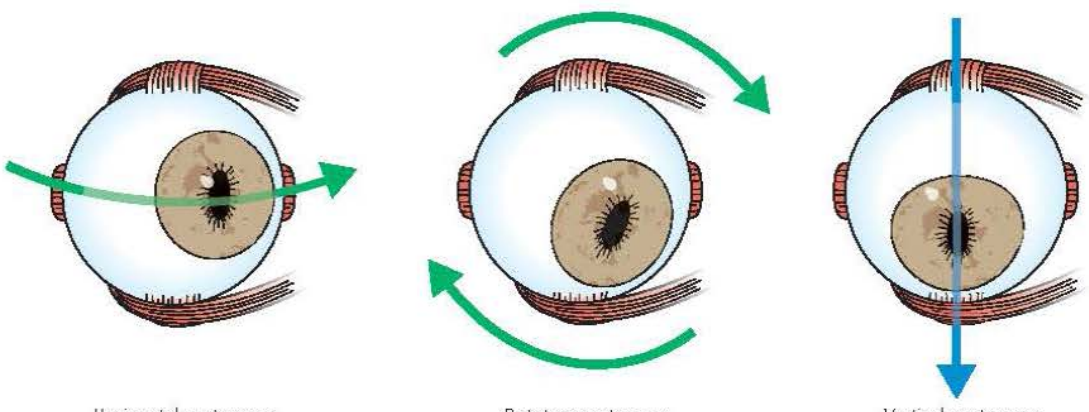
In the absence of any head movement, nystagmus should never be present in a normal animal. Two types of pathological nystagmus can be observed with vestibular disorders:

- **Spontaneous** (observed when the head is in a normal position at rest), and/or
- **Positional**, which occurs when the head is held in different positions (e.g. to either side, dorsally or by placing the animal upside down on its back).

Nystagmus is usually classified on the basis of its direction (the fast movement) and may be horizontal, vertical or rotatory. By convention, the direction of the nystagmus is described according to the direction of its fast phase. This can be confusing, because the lesion is present on the side of the slow phase of the nystagmus (i.e. a horizontal nystagmus with the fast phase to the right side is usually indicative of a left-sided lesion of the vestibular system).

As opposed to jerk nystagmus, in which the nystagmus has a slow and fast phase, pendular nystagmus is characterized as a continuous oscillation of both globes without slow or fast components; less commonly, it may be characterized as random eye movements (amaurotic or 'searching' nystagmus). This type of nystagmus is not associated with vestibular disease and may occur secondary to congenital abnormalities of the visual pathways in Siamese, Birman and Himalayan cats, as well as in Belgian Shepherd Dogs.

▼ 195 **Pathological jerk nystagmus results from a unilateral disturbance in the normal bilaterally tonic influences provided by vestibular neurons to the motor nuclei of the extraocular muscles (CNs III, IV, VI). Spontaneous or positional horizontal or rotatory jerk nystagmus can be seen with either central or peripheral vestibular syndrome. Spontaneous or positional vertical nystagmus or nystagmus that changes direction indicates the presence of central vestibular syndrome.**





▶ **196** **Positional strabismus in the left eye of a Rottweiler with a central vestibular syndrome. This strabismus was only visible by placing the head in extension, indicating a sensory dysfunction (vestibular apparatus) rather than a motor one (abnormal innervation of the extraocular muscles by CNs III, IV and VI).**

Other clinical signs of vestibular disease include:

- **Positional strabismus**, which can be seen associated with vestibular disease when the head is placed in an abnormal position (extended dorsally or the animal placed on its back). Vestibular disease often causes a ventral or ventrolateral positional strabismus in the eye ipsilateral to the vestibular lesion (**196**).
- **Ataxia** is caused by a lack of vestibular input to the ipsilateral limb extensor muscles. This results in swaying of the trunk and head, leaning, falling and rolling to one side with a unilateral lesion. The animal may tend to circle towards the affected side. These circles are usually small, which will appear as though the patient is falling in that direction. The laterally recumbent animal prefers to lie on the side of the body with the lesion and the ipsilateral limb often has decreased extensor tone. With bilateral vestibular disease, affected animals tend to fall to either side and they often show wide excursions of the head from side to side.
- **Leaning, falling and a wide-based stance.** The vestibular system affects limb tone via the vestibulospinal tract, which facilitates the ipsilateral extensor muscles and is a source of inhibition of the contralateral extensor muscles. With unilateral vestibular disease, the lack of vestibular input can result in the animal leaning and falling on the affected side as a result of the ipsilateral limb having decreased extensor tone and the contralateral side limbs having increased extensor tone. With bilateral vestibular disease, the animal falls to either side and often adopts a wide-based stance. The latter is also seen with cerebellar disease.

Animals with acute vestibular disease may additionally display vomiting associated with dysequilibrium.

NEUROLOGICAL EVALUATION

The presence of a head tilt and jerk nystagmus is indicative of vestibular disease. The primary goal for a clinician examining a patient with head tilt and jerk nystagmus is to determine whether the patient has evidence of peripheral or central vestibular disease, as the differential diagnoses, diagnostic and treatment considerations and prognoses differ.

Is it a peripheral or a central vestibular disease?

Both peripheral and central vestibular disease can cause a head tilt, horizontal or rotatory nystagmus, positional strabismus and ataxia. Most lesions causing vestibular disease affect a region rather than a specific nerve or nucleus, so accompanying neurological abnormalities can often be used to localize the lesion to the peripheral or central vestibular system.

Correctly identifying central vestibular disease requires identification of clinical signs not attributable to diseases of the peripheral vestibular system. However, even if such signs are not present, a central lesion cannot be excluded. Lesions that affect the central vestibular system typically have additional clinical signs suggestive of brainstem involvement. Such lesions often involve the reticular formation as well as ascending and descending motor and sensory pathways to the ipsilateral limbs. Therefore, abnormal mental status (depression, stupor, coma), ipsilateral UMN hemiparesis and GP ataxia, and conscious proprioceptive deficits are

commonly associated with central vestibular disease. Deficits of CNs V to XII (other than VII and VIII) can also be associated with central vestibular disease. The presence of spontaneous or positional jerk nystagmus indicates vestibular dysfunction but does not further localize the lesion to the peripheral or central vestibular system. However, vertical nystagmus and nystagmus that changes in direction on changing position of the head (i.e. variable nystagmus) are features of central vestibular lesions. The rate of nystagmus (number of beats per minute with the head in a neutral position as well as with the animal in dorsal recumbency) can further assist with differentiation between central vestibular disease and peripheral vestibular disease. According to one study, the median rate of resting and positional nystagmus appears to be significantly faster for dogs with peripheral vestibular disease with a resting nystagmus ≥66 bpm, providing the highest combined sensitivity and specificity in diagnosing peripheral vestibular disease. In this study, the median rates for resting and positional nystagmus in dorsal recumbency were 0 and 30 bpm for dogs with central vestibular disease and 90 and 120 bpm for dogs with peripheral vestibular disease, respectively.

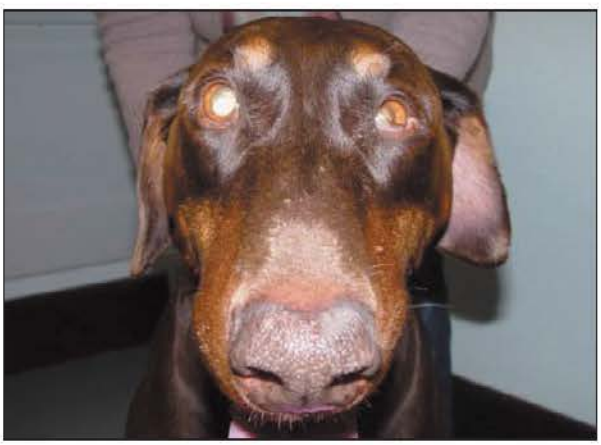
Identification of ear disease (**197**), facial nerve paralysis and/or Horner's syndrome (**198**) is suggestive of peripheral vestibular disease due to the proximity of CN VII (facial nerve) and the ocular sympathetic nerve supply, with the vestibular nerve in the region of the petrous temporal bone.

Pitfalls of lesion localization in vestibular disease

Occasionally, intracranial vestibular lesions can result initially in signs indicative of a peripheral lesion. This is most commonly seen with extra-axial masses that compress CN VIII as it exits the brainstem and lesions that involve solely the vestibular nuclei. In the absence of involvement of the UMN and GP systems adjacent to the central vestibular nuclei in the caudal brainstem, these lesions cause ipsilateral clinical signs similar to all the lesions that affect the peripheral components of the vestibular system. If in doubt about the localization of the lesion, the clinician should investigate the animal for central vestibular disease as well as peripheral vestibular disease. Conversely, animals with acute, severe peripheral vestibular disease may be so incapacitated that accurate interpretation of neurological examination findings may not be possible.



▲ **197** Left-sided facial nerve paralysis in a Boxer with otitis media. Because of the close association of the facial and vestibulocochlear nerves, they often are affected simultaneously by the same lesion.



▲ **198** Horner's syndrome (miosis, enophthalmos, protruded third eyelid on the left side of this dog with middle ear disease) can be seen with peripheral vestibular disease due to the proximity of the sympathetic nerve supply to the eye to the vestibular nerve and receptor in the region of the petrous temporal bone.

With both central and peripheral vestibular disease, the head tilt, circling and nystagmus typically occur ipsilateral to the side of the lesion. Less frequently, lesions affecting the caudal cerebellar peduncle, the fastigial nucleus and/or the flocculonodular lobes of the cerebellum can cause central vestibular disease, resulting in a paradoxical head tilt. The syndrome is described as 'paradoxical' because the head tilt and loss of balance occur contralateral to the side of the central lesion. There is also usually some evidence of a cerebellar disorder, such as a cerebellar ataxia (e.g. ipsilateral hypermetria) or a truncal sway. In this situation, the lesion occurs ipsilateral to the UMN paresis and/or hypermetria.

Bilateral vestibular disease is characterized by a head sway from side to side, loss of balance on either side and symmetrical ataxia with a crouched posture closer to the ground surface. A physiological nystagmus cannot usually be elicited and a head tilt is not observed. Bilateral vestibular disease can occur as a result of a lesion affecting both peripheral vestibular components or, less commonly, both central vestibular components. As with unilateral vestibular disease, the presence of signs that cannot be attributed to diseases of the peripheral vestibular system (abnormal mental status, postural reaction deficits, paresis, vertical or variable nystagmus) can be used to differentiate bilateral central vestibular disease from bilateral peripheral vestibular disease.

In very rare cases, vestibular disease may be part of a diffuse polyneuropathy or cranial polyneuropathy. Other CN dysfunction, such as dysphagia, tongue weakness, jaw weakness and/or facial paralysis, as well as limb weakness with depressed segmental spinal reflexes, may be seen.

Lesions of the thalamus (**199**), extrapyramidal basal nuclei and rostral mesencephalon may also cause head tilt and signs of central vestibular disease, with involvement of the vestibular thalamic area (ventromedial thalamic nucleus, thalamic reticular nucleus and ventral lateral geniculate complex) and its afferent connections with the brainstem vestibular nuclei (medial longitudinal fasciculus). Head tilt in the absence of other signs of vestibular disease may also be seen with lesions affecting the rostral aspect of the brainstem or caudal aspect of the thalamus. Although the mechanism is unclear, such lesions may cause an increase in activity of the major ipsilateral dorsal neck muscles and in contralateral obliquus capitis caudalis muscles.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis list is entirely dependent on the anatomical diagnosis. A lesion must therefore be localized to a particular section of the vestibular apparatus (i.e. peripheral or central vestibular apparatus) before an appropriate differential diagnosis list can be established and further testing conducted. The differential diagnosis list can be further developed taking into account historical findings. A thorough history should be obtained to gain information with respect to the onset and progression of the disease, any history of trauma, vaccination history, presence of other clinical signs, history of ear disease and whether potentially ototoxic drugs or drugs that can affect the function of the central vestibular system have been administered.

Disease mechanisms and conditions commonly seen in an emergency evaluation of a dog or a cat with vestibular disorder are outlined in the *Tables 63* and *64*.



▲ **199** **Dorsal plane T2-weighted MR image of the brain of a 7-year-old Greyhound with a rostromedial thalamic lacunar infarct (arrow) simultaneously affecting the internal capsule. This region is supplied by the proximal perforating artery. This dog presented acutely with signs of ataxia, with leaning and falling to the contralateral side of the lesion.**

Table 63 **Causes of peripheral vestibular disease**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Otitis media*/interna* Nasopharyngeal polyps (rare)	Otitis media*/interna* Nasopharyngeal polyps*
Trauma	Head trauma*	Head trauma*
Toxic	Aminoglycosides*, topical iodophors or chlorhexidine*	Aminoglycosides*, topical iodophors or chlorhexidine*
Anomalous	Congenital vestibular disease	
Metabolic	Hypothyroidism	
Idiopathic	Acute idiopathic peripheral vestibular disease*	Acute idiopathic peripheral vestibular disease*
Neoplastic	Middle and/or inner ear tumour	Middle and/or inner ear tumour

* Common cause

Table 64 **Causes of central vestibular disease**

DISEASE MECHANISM	DOGS	CATS
Vascular	Brain infarct* Brain haemorrhage	Brain infarct Brain haemorrhage
Inflammatory/infectious	Infectious encephalitis (distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial)* Meningoencephalitis of unknown aetiology (GME, necrotizing, idiopathic)*	Infectious encephalitis (*Toxoplasma*, bacterial, FIP, *Cryptococcus*)* Meningoencephalitis of unknown aetiology (presumed immune mediated)
Trauma	Head trauma*	Head trauma
Toxic	Metronidazole toxicity*	Metronidazole toxicity
Anomalous	Intracranial intra-arachnoid cyst Dermoid/epidermoid cyst Dandy–Walker syndrome Chiari-like malformation (rare) Hydrocephalus	Intracranial intra-arachnoid cyst Dermoid/epidermoid cyst
Neoplastic	Primary or metastatic brain tumour*	Primary or metastatic brain tumour
Nutritional	Thiamine deficiency	Thiamine deficiency

* Common cause

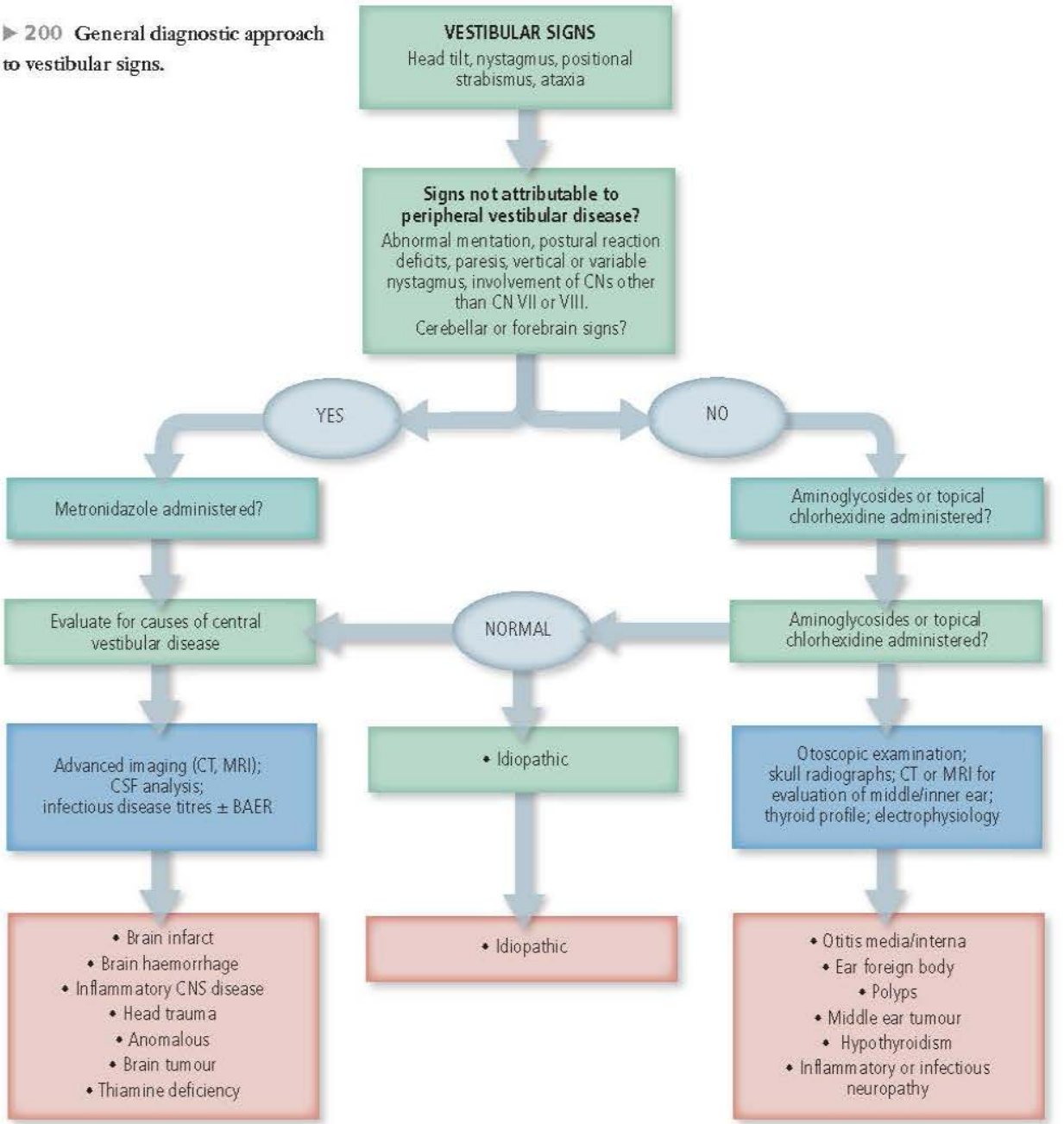
Specific diagnostic tests

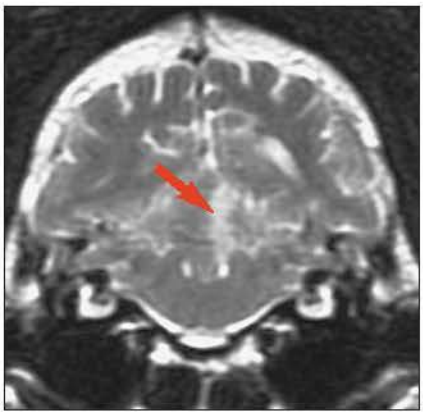
The choice of neurodiagnostic tests in patients with vestibular disease depends essentially on where the lesion is suspected to be on the basis of the neurological examination. If in doubt about the localization of the lesion, the animal should be evaluated for both peripheral and central vestibular disease (**200**).

Peripheral vestibular disease

- **Otoscopic and pharyngeal examination** under GA (particularly to check for possible inflammatory polyps in cats).
- **Swabs** for cytology and culture (aerobic, fungal and yeast) from the middle ear if the tympanic membrane is ruptured.

▶ **200 General diagnostic approach to vestibular signs.**





▲ **201** Cerebellar infarct is a potential cause of acute central vestibular syndrome. This T2-weighted MR image of the caudal fossa shows a border zone cerebellar infarct (arrow) at the junction between the median and intermediate rostral cerebellar arteries.

- **Myringotomy** with a 20-gauge spinal needle to obtain samples for cytology and culture if the tympanic membrane is intact, but bulging or of an abnormal colour.
- **Imaging of the tympanic bullae** with radiographs, CT or MRI to assess for otitis media/interna and polyps.
- **Thyroid function testing.** Serum T4, free T4 and endogenous canine serum TSH determinations, and if these are suggestive but inconclusive for hypothyroidism, they can be followed by a TSH stimulation test.
- **BAER** test to help differentiate central from peripheral vestibular disease if needed.
- **EMG** and motor nerve conduction study indicated in patients suspected of cranial polyneuropathy or of a more diffuse polyneuropathy.

Central vestibular disease

- **Advanced brain imaging** (CT or MRI) (**201**).
- **CSF analysis** (nucleated cell count, cytology and total protein concentration).
- **Serum and CSF** infectious titres (serology and/or PCR) for various infectious organisms (*Toxoplasma gondii*, *Neospora caninum*, canine distemper, coronavirus, rickettsial, *Cryptococcus* and *Aspergillus*).

COMMON CAUSES OF ACUTE PERIPHERAL VESTIBULAR DISEASE

Acute idiopathic peripheral vestibular syndrome

Overview

This syndrome affects both cats and dogs. It is most prevalent in geriatric dogs and is rarely observed before 5 years of age. It has been reported in the late summer in young cats with access to the outdoors in the northeastern US, where it has been hypothesized (with no definitive proof) that this condition is caused by migration of *Cutebra* spp. larvae through the nasal cavity and cribriform plate of the ethmoid bone to enter the cranial cavity. There is no known cause in dogs.

Clinical presentation

Animals present with acute and non-progressive signs of peripheral vestibular disease. Affected animals tend to appear extremely disabled in the first 48–72 hours, making a neurological examination very difficult. No other neurological signs are observed.

Diagnosis

Diagnosis is made by exclusion of other causes of acute peripheral vestibular disease.

Management

Affected animals usually improve dramatically in 1–3 weeks from the onset of signs. The nystagmus usually resolves quickly (within the first few days). Improvements in posture and walking occur within 7 days, whereas a head tilt tends to be the last sign to improve and may be residual. The recovery probably occurs as a combination of substitution of visual and somatosensory cues for the lost vestibular cues and adaptation of the vestibular system by modulation of activity in the brainstem and cerebellum.

No treatment has been proven beneficial. Meclizine (12.5 mg PO q12h in dog; 6.25 mg PO q12h in cats), diazepam (0.1–0.5 mg/kg PO q8h in dogs; 1–2 mg PO q12h in cats) and/or maropitant (1 mg/kg SC q24h or 2 mg/kg PO q24h in dogs) are sometimes helpful in decreasing signs associated with acute vestibular disorder (nausea, anorexia, anxiety and, in some instances, the severity of the head tilt and ataxia).

Some animals may be left with episodic ataxia or a persistent head tilt. Recurrence occasionally occurs after a variable period of weeks to months.

Otitis media/interna

Overview

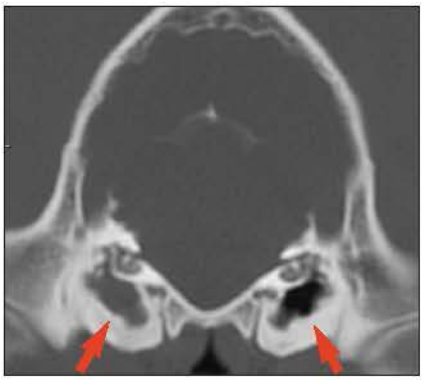
Otitis media/interna is usually associated with chronic otitis externa/media, nasopharyngeal infection extending through the auditory tube or haematogenous dissemination from a bacteraemia. The condition may arise in the absence of external ear canal inflammation.

Clinical presentation

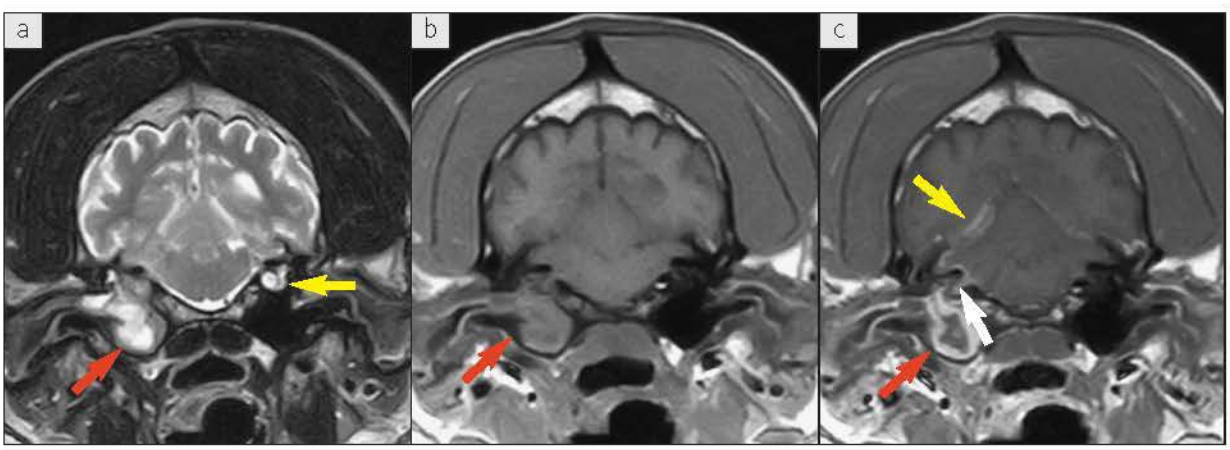
Clinical signs can be acute or chronic in onset and progressive and can be associated with ipsilateral facial paralysis and/or 3rd order Horner's syndrome.

Diagnosis

Diagnosis is based on otoscopic examination and imaging studies (bullae radiographs, CT [**202**] or MRI [**203**]) and/or exclusion of other causes of peripheral vestibular disease. Myringotomy (for culture and sensitivity) is indicated if fluid is present in the middle ear.



▲ **202** **CT scan at the level of the temporomandibular joint displayed in a bone window, showing bilateral marked thickening of both tympanic bulla walls (arrows). The normally air-filled tympanic bullae are partially (right side) and completely (left side) occupied by soft tissue/fluid material. These findings are strongly suggestive of bilateral chronic otitis media.**



▲ **203** **MR images of a 5-year-old Cocker Spaniel with right-sided otitis media/interna with secondary meningoencephalitis causing central vestibular signs. (a) On the transverse T2-weighted image, the right bulla contains tissue (red arrow) that is mostly hyperintense to neural tissue. Fluid within the membranous labyrinth of the normal left inner ear is visible as a curved structure with a high signal (yellow arrow), while there is a partial lack of the high fluid signal from the right inner ear. (b) On the transverse T1-weighted image, the normal left bulla is visible as a signal void because it contains air. The right bulla contains tissue that is isointense to neural tissue (arrow). (c) Following intravenous administration of gadolinium-DTPA, the tissue filling up the bulla shows marked uptake of contrast in its periphery (red arrow). There also is marked enhancement of the vestibulocochlear nerve (white arrow) and meninges overlying the cerebellum (yellow arrow).**

Management

Treatment consists of systemic antibiotics for a minimum of 4–6 weeks. The choice of antibiotic is dictated by results of culture/sensitivity if available; if not, amoxicillin/clavulanate, cephalosporin or fluoroquinolones are reasonable choices to consider. Potentiated sulphonamides should be avoided if there is associated facial paralysis due to the development (however limited) of keratoconjunctivitis sicca.

Surgical drainage and debridement via bulla osteotomy may be required if the patient is refractory to medical treatment.

The prognosis is good for resolution of the infection, but neurological deficits such as mild head tilt, facial paralysis or Horner's syndrome may persist despite effective therapy because of permanent damage to the neural structures. The presence of persistent nystagmus is suggestive of an active disease process.

Occasionally, an infection can extend into the cranial vault from the middle and inner ear, causing central vestibular disease rather than peripheral vestibular disease.

Nasopharyngeal polyps in cats

Overview

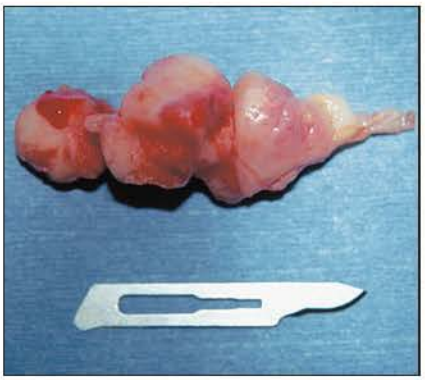
Nasopharyngeal polyps are frequently seen in young adult cats. They originate from the auditory tube or lining of the bulla. Evidence of otitis externa is often present. Otitis media/interna can be a complication. The polyps can also be associated with facial nerve paralysis and/or 3rd degree Horner's syndrome.

Diagnosis

Diagnosis is based on visualization of the polyp in the external ear canal or nasopharynx and imaging in refractory otitis media/interna. Histopathology is necessary to confirm the diagnosis.

Management

Treatment consists of polyp removal with simple traction or surgery via ventral bulla osteotomy (**204**). Antibiotics are usually not recommended unless an associated bacterial infection is identified based on results of culture/sensitivity. The prognosis is good, but recurrence is possible.



▲ **204** **Nasopharyngeal polyp removed from the tympanic bulla via ventral bulla osteotomy in a cat with peripheral vestibular syndrome and facial nerve paralysis. (Photo courtesy Jonathan Bray)**

COMMON CAUSES OF ACUTE CENTRAL VESTIBULAR DISEASE

Brain infarct

See Chapter 17.

Metronidazole toxicity

Overview

Metronidazole neurotoxicosis is mostly seen with long-term administration, usually at high doses (exceeding 60 mg/kg/day in dogs and cats, although doses as low as 30 mg/kg/day have been responsible) and occasionally as soon as 3 days after starting treatment.

Anorexia and vomiting are frequent initial clinical signs. The condition progresses rapidly to bilateral central vestibular disease with symmetrical or asymmetrical signs. Spontaneous recovery occurs within 3–14 days following drug withdrawal. Diazepam (initially 0.5 mg/kg IV bolus then PO q8h for 3 days) may enhance the speed of recovery.

Meningoencephalitis of unknown aetiology

See Chapter 19.

ACUTE DISORDERS OF THE HEAD AND FACE

Lara Matiasek & Alberta de Stefani

INTRODUCTION

Acute disorders of the head and face can range in severity from benign to life threatening. Their recognition, based on typically characteristic signs, can help define a lesion localization and identify a differential diagnosis list.

The majority of such disorders are due to diseases affecting the CNs in either their peripheral or their central (brainstem) location. Some of the disorders are manifestations of more diffuse NM diseases. Although the recognition of a CN abnormality may be achieved rapidly following visual inspection of the patient, the precise location of the disease can only be determined by a thorough neurological examination. Such localization is necessary to ensure consideration is given to the most appropriate diagnostic tests.

Some of the conditions affecting the head and face are described in other chapters. These include vestibular abnormalities causing head tilt and nystagmus (Chapter 14), ophthalmological abnormalities causing blindness (Chapter 12) and tetanus and botulism causing trismus and multiple cranial neuropathies, respectively (Chapter 25). The acute abnormalities affecting the head and face discussed in this chapter include anisocoria, trismus, dropped jaw, masticatory muscle atrophy, facial paralysis, stridor/dysphonia and dysphagia/regurgitation.

ANISOCORIA

Introduction

The pupil is an important indicator of the neurological health of the central and peripheral nervous systems. The pupil regulates the amount of light that reaches the retina via the sympathetic and parasympathetic nerve pathways that innervate the iris. The pupil size is in a constant state of flux, a result of a labile, dynamic equilibrium between the sympathetic and parasympathetic innervations. When presented with an animal with pupils of unequal size (anisocoria) or shape (dyscoria), a primary or secondary anatomical or mechanical pupil abnormality must be investigated before consideration is given to a neurological dysfunction. Examples of primary or secondary anatomical or mechanical disorders include iris atrophy, uveitis, glaucoma, subluxated lenses and synechiae.

Neuroanatomical basis

Two systems are implicated in the control of pupil size: the parasympathetic system and the sympathetic system.

Parasympathetic innervation of the eye and pupil constriction

The ocular parasympathetic tract is a two-neuron pathway mediated by the parasympathetic component of the oculomotor nerve (CN III) (see **181**), which is involved in the control of pupillary constriction. The motor portion of the oculomotor nerve is responsible for innervation of the levator palpebrae superioris (responsible for elevation of the upper eyelid) and the ipsilateral dorsal, ventral and medial recti, as well as the ventral oblique muscle (extraocular muscles responsible for movement of the eyeball).

Parasympathetic denervation of the pupil (internal ophthalmoplegia) can occur with or without disturbing the motor innervation of the oculomotor nerve (external ophthalmoplegia).

Internal ophthalmoplegia

The clinical signs of internal ophthalmoplegia include a widely dilated pupil that is non-reactive to direct and indirect light stimulation. The associated anisocoria is particularly obvious in ambient light, while maximal and equal dilation of both eyes occurs on dark adaptation. Common causes include pharmacological blockade with atropine or atropine-like compounds, middle cranial fossa syndrome (also known as cavernous sinus syndrome), mesencephalic lesions, ipsilateral cerebellar lesions and orbital diseases.

External ophthalmoplegia

Clinical signs of external ophthalmoplegia include ptosis of the upper eyelid and lateral strabismus with an inability to move the globe dorsally, ventrally or medially, plus/minus signs of internal ophthalmoplegia. Common causes include middle cranial fossa syndrome, extraocular myositis, fibrosing esotropia, trauma and retrobulbar lesions.

Sympathetic innervation of the eye and pupil dilation

The ocular sympathetic tract is a three-neuron pathway (**205**). The central, or UMN, pathway begins in the hypothalamus and descends in the spinal cord through the lateral tectotegmentospinal tract to synapse on the LMN at the level of the T1–T3 spinal cord segments. The LMN is divided into a pre-ganglionic and post-ganglionic neuron. The pre-ganglionic axons leave the spinal nerve in the segmental ramus communicans, which joins the thoracic sympathetic trunk inside the thorax ventrolaterally to the vertebral column. It then continues cranially along the cervical sympathetic trunk, where it is part of the vagosympathetic trunk within the carotid sheath. It then synapses with the bodies of the post-ganglionic cells in the cranial cervical ganglion, which lies caudal to the tympanic bulla. Post-ganglionic axons enter the middle ear and then the middle cranial fossa, where they join the ophthalmic branch of the trigeminal nerve running to the orbit. The sympathetic nervous system innervates and provides tone to the smooth muscle of the eye and eyelids. This tone keeps the eyeball protruded, the eyelids opened and third eyelid retracted, causing the palpebral fissure to widen and the third eyelid to be pulled ventromedially. The tone of the iris dilator muscle is also maintained by the sympathetic system, which keeps the pupil partially dilated under normal conditions and dilates it during periods of darkness, stress, fear and painful stimuli.

▼ **205** **Schematic representation of the neuroanatomy of the sympathetic nerve supply to the eye (Horner's pathway).**

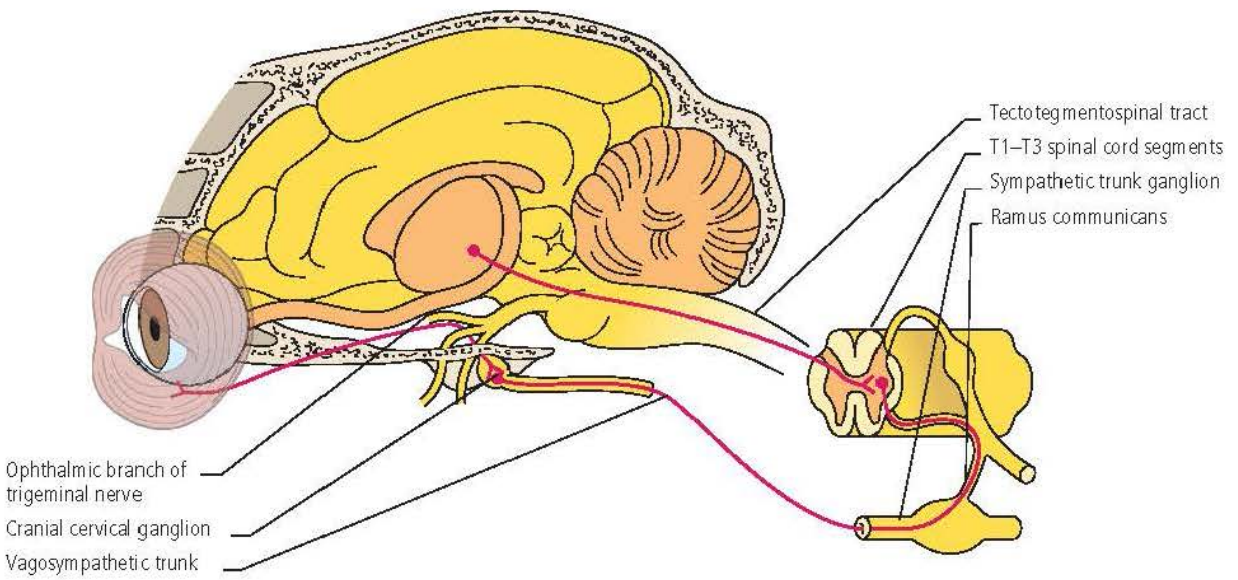


Table 65 **Pharmacological tests of lesion level in parasympathetic/sympathetic denervation**

DRUG	AFFECTED EYE			NORMAL EYE
Parasympathetic denervation	PRE-GANGLIONIC LESION		POST-GANGLIONIC LESION	
Pilocarpine 0.1%	Constriction occurs more slowly, similar to the normal eye		Rapid constriction of the pupil compared to normal eye due to denervation hypersensitivity	20–30 minutes in dogs/cats
Physostigmine 0.5%	Rapid constriction of the pupil compared to normal eye		No effect on pupil size	Constriction in 40–60 minutes
Sympathetic denervation	FIRST ORDER	SECOND ORDER (PRE-GANGLIONIC)	THIRD ORDER (POST-GANGLIONIC)	
Phenylephrine 1%	Dilation in 60–90 minutes	Dilation in 20–45 minutes	Dilation in less than 20 minutes	Dilation in about 90 minutes in dogs. Minimal effect in cats

Note: A complete absence of pupillary response after administration of pilocarpine 0.1% in the pathological eye (pupil continues to be mydriatic) probably suggests a non-neurological cause (i.e. iris atrophy).

Sympathetic denervation of the eye results in Horner's syndrome. Clinical signs include miosis, drooping of the upper eyelid (ptosis), enophthalmia and protrusion of the third eyelid. Damage anywhere along the sympathetic pathway can cause Horner's syndrome. This syndrome is most commonly observed with lesions affecting the post-ganglionic fibres (secondary to otitis media, middle ear neoplasia, orbital disease and idiopathic dysfunction) or pre-ganglionic fibres (brachial plexus tumour or injury, cranial mediastinal mass, neck injury). Horner's syndrome is usually described as first order (central pathways), second order (pre-ganglionic) or third order (post-ganglionic) according to the level of the lesion along the sympathetic pathway.

Neurological evaluation

The clinical approach to anisocoria involves the following steps:

- Ophthalmological examination to rule- out non-neurological causes (primary or secondary anatomical or mechanical pupil abnormalities).
- Determining which pupil is abnormal by checking the PLR and determining if the asymmetry in pupil size increases in bright light or in darkness.
- Determining if the lesion is pre-ganglionic or post-ganglionic by pharmacological testing (*Table 65*) and looking for other neurological signs (see *Table 66*, next page).

Differential diagnosis

The differential diagnosis and disease mechanisms often encountered in dogs or cats with anisocoria are listed in *Table 66*.

Table 66 **Features of anisocoria in dogs and cats**

Lesion localization	Pupil abnormality	Associated signs	Differential diagnoses	Diagnostic tests
Sympathetic supply to the eye (Horner's syndrome)	Ipsilateral miosis, intact PLR bilaterally	Anisocoria most obvious in darkness; third eyelid protrusion; enophthalmos; ptosis of upper eyelid; normal vision	• Middle ear disease • Idiopathic • Cervical/rostral thoracic spinal lesions • Brachial plexus lesion • Injuries to soft tissues of the neck • Skull fractures • Retrobulbar lesion	• Pharmacological test with phenylephrine 1% • First order: CT/MRI brain and cervical area • Second order: CT/MRI cervical area and brachial plexus, chest radiographs • Third order: otoscopic examination, CT/MRI of bullae
Parasympathetic component of oculomotor nerve (CN III)	Severe ipsilateral mydriasis, absent direct and indirect PLR	Anisocoria most obvious in light; narrowing of the palpebral fissure due to ptosis of upper eyelid; normal vision – ventrolateral strabismus and reduced ocular mobility if motor component of CN III involved	• Dysautonomia • Cerebrovascular accident • Inflammatory disease • Neoplastic disease	• Pharmacological test with pilocarpine 0.1% or physostigmine 0.5% • CT/MRI of brain
Unilateral retinal lesion	Partial ipsilateral mydriasis, absent direct PLR, normal indirect PLR	Pupils symmetrically dilated in darkness, fundoscopic examination and ipsilateral vision abnormal	• Inflammatory disease • Neoplastic disease • Retrobulbar contusion • Congenital abnormalities (optic nerve hypoplasia) • Degenerative diseases	• Fundoscopic examination • ERG • Ocular ultrasound
Unilateral optic nerve lesion	Partial ipsilateral mydriasis, absent direct PLR, normal indirect PLR	Pupils symmetrically dilated in darkness, ipsilateral vision abnormal	• Neoplastic disease • Inflammatory disease	• Fundoscopic examination • ERG • CT/MRI of orbit and brain • CSF analysis
Optic chiasm	Absent PLR in both eyes	Absent vision bilaterally, also likely forebrain signs (e.g. depression, compulsive gait, proprioceptive deficits)	• Neoplastic disease • Inflammatory disease • Cerebrovascular accident (rare)	• CT/MRI of brain • CSF analysis
Unilateral optic tract (rostral/proximal to the lateral geniculate nucleus)	Contralateral pupil remains more dilated during swinging flashlight test. Both pupils dilate normally in the dark	Homonymous hemianopia (loss of medial visual field in one eye and of the lateral visual field in the other eye). Vision is mostly affected in the eye opposite the lesion. Other forebrain signs are probably associated	• Inflammatory disease • Neoplastic disease • Cerebrovascular accident • Trauma	• CT/MRI of brain • CSF analysis

(Continued)

Table 66 Features of anisocoria in dogs and cats *(continued)*

Lesion localization	Pupil abnormality	Associated signs	Differential diagnoses	Diagnostic tests
Unilateral visual cortex	Normal PLRs in both eyes. Normal ability to dilate pupil in darkness	Homonymous hemianopia or complete blindness in the eye opposite the lesion. Other forebrain signs are probably associated	• Cerebrovascular accident • Inflammatory disease • Neoplastic disease	• CT/MRI brain • CSF analysis
Cerebellar lesion	Ipsilateral miosis or contralateral mydriasis	Menace response deficit with normal vision, intention tremor, hypermetric gait, vestibular signs		• CT/MRI brain • CSF analysis

Common causes of anisocoria

Horner's syndrome

Overview

Horner's syndrome is a condition caused by a decreased sympathetic supply to the eye. It has been described in dogs and cats. Due to its very long pathway, many disease processes may affect the sympathetic supply to the eye. Among the most common causes of Horner's syndrome are the idiopathic form, middle ear diseases, trauma to the neck or brachial plexus and mediastinal masses.

Clinical presentation

Typical clinical signs include a miotic pupil, ptosis of the upper eyelid, protrusion of the third eyelid, enophthalmos and conjunctival hyperaemia (**206**).



▲ **206** **Mixed-breed dog with right-sided miosis, third eyelid protrusion and ptosis compatible with Horner's syndrome.**

Horner's syndrome is usually classified based on the level of the lesion along the sympathetic pathway (first, second and third order). Phenylephrine eye drops 1% can be helpful in testing this level (*Table 65*). Pharmacological testing should always be performed in both eyes, using the normal eye as a comparison.

Neurological signs present in association with Horner's can help localize the lesion:

- **First-order Horner's syndrome** (rare). Signs associated with the intracranial portion: altered mental status; changes in behaviour; abnormal temperature regulation; endocrine disturbances; visual deficits. Signs associated with the cervical intramedullary portion: ataxia, paresis/plegia (usually mono- or hemi-paresis/plegia); postural reaction deficits ipsilateral to the Horner's syndrome in one limb, in limbs on the same side, or in all four limbs.
- **Second-order Horner's syndrome.** Signs associated with the intramedullary/brachial plexus portion: weakness, paresis/plegia affecting one limb (monoparesis/plegia), all four limbs (tetra-paresis/plegia), or only the limbs on the side of the Horner's syndrome (hemi-paresis/plegia); postural reaction deficits (usually) in the forelimb ipsilateral to the Horner's syndrome; reduced reflexes in the forelimb (usually) ipsilateral to the Horner's syndrome or in both forelimbs; depressed or absent ipsilateral cutaneous trunci reflex. Signs associated with the cervical portion: laryngeal dysfunction (rare).
- **Third-order Horner's syndrome.** Can commonly see facial paralysis and/or peripheral vestibular signs.

Diagnosis

Diagnosis of Horner's syndrome is based on clinical signs. Further investigations are warranted to identify the underlying cause. The following diagnostic tests can be performed in dogs or cats:

- **First-order Horner's syndrome.** MRI of the brain and cervical spine to T4; CSF analysis.
- **Second-order Horner's syndrome.** CT or thoracic radiographs, MRI of the brachial plexus and CT/MRI/ultrasound of the cervical area.
- **Third-order Horner's syndrome.** Radiographs/CT/MRI of the tympanic bullae and MRI of the brain.

Management

Treatment and prognosis for Horner's syndrome are generally dependent on the underlying cause, though the prognosis is generally excellent for the idiopathic form.

Dysautonomia

Overview

Dysautonomia is due to autonomic nervous system failure and has been described in both dogs and cats. While in the 1980s this condition was mainly documented in the UK, its distribution is now worldwide. The aetiopathogenesis of this disease is not entirely clear. A possible autoimmune basis has been suspected in some dogs with co-existing autoimmune MG and dysautonomia. Evidence of *Clostridium botulinum* type C toxin and antibodies to both the toxin and the surface antigens of *C. botulinum* were identified in a group of cats affected by dysautonomia. This supports the implication of *C. botulinum* type C/D in the pathogenesis of dysautonomia. In dogs the only identified risk factors for developing dysautonomia include living in rural areas and spending more than 50% of time outdoors.

Clinical presentation

Clinical abnormalities typically reflect signs of autonomic nervous system (sympathetic and parasympathetic) dysfunction. Common clinical signs in cats include vomiting/retching, depression, anorexia, third eyelid protrusion, dilated non-responsive pupils, dry eyes and nose, constipation (sometimes with faecal impaction) and dehydration (**207, 208**). Urinary and faecal incontinence have been observed. Bradycardia and megaoesophagus are often present.

Common clinical signs in dogs include lethargy, anorexia, retching, regurgitation/vomiting, hypersalivation and diarrhoea or, occasionally, constipation. Dry mucous membranes, dry eyes and nose are often seen, as well as dilated or anisocoric pupils. Other signs include megaoesophagus, decreased anal tone and distended, atonic urinary bladder and bradycardia.



▲ 207 A young cat with bilateral third eyelid protrusion.



▲ 208 A young dog with bilateral mydriasis and third eyelid protrusion.

Diagnosis

Diagnosis *in vivo* is based on the presence of typical clinical signs. Several pharmacological tests can be performed to support the clinical diagnosis. The ocular pharmacological test using pilocarpine 0.1% is very helpful in confirming a post-ganglionic parasympathetic lesion. In dysautonomic patients there is rapid development of miosis (due to denervation hypersensitivity) after instillation of 1 or 2 drops of pilocarpine 0.1%.

In patients exhibiting dysuria, the bethanechol challenge test can be performed; after subcutaneous administration of a low dose (0.04 mg/kg), dysautonomic patients often show an improved ability to urinate. Other (less common) pharmacological tests include assessing a flare response to intradermally administered histamine or monitoring the heart rate response to intravenous or subcutaneous atropine injection. In both cases a diminished response is expected in dysautonomic patients.

Decreased urinary catecholamine measurements can also support a diagnosis of dysautonomia, as it is indicative of denervation hypersensitivity. Documenting orthostatic hypotension can highlight failure of the sympathetic heart innervation and has been used in dogs to diagnose autonomic failure.

The diagnosis can be confirmed by histopathology. The lesions primarily involve the neuronal cell bodies of the autonomic ganglia of both the sympathetic and parasympathetic systems. These lesions are characterized by chromatolytic changes in the autonomic neurons, neuronal degeneration and loss, neuronophagia and, occasionally, mild mononuclear perivascular cuffing.

Management

Therapy for dysautonomia is only supportive. Correction of hypovolaemia and/or electrolyte abnormalities is recommended. Metoclopramide (0.2–0.5 mg/kg IM, SC or PO q6–8h) enhances gastrointestinal motility and bethanechol (2.5–25 mg/dog orally q8h and 1.25–5.0 mg/cat or 0.1–0.2 mg/kg PO q8h) can be used to help evacuate the bladder. Gastrostomy tubes need to be considered for long-term nutrition in patients with megaoesophagus. The administration of ocular pilocarpine can improve lacrimal and oral secretion. The prognosis in both dogs and cats is guarded to poor.

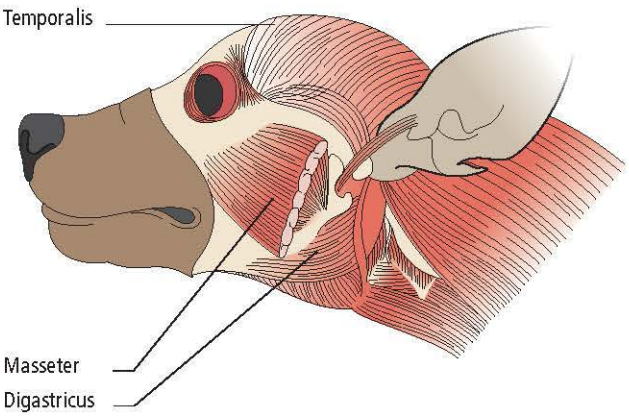
TRISMUS

Introduction

Trismus (also called 'lockjaw') describes a limited ability to open the mouth due to spasm of the jaw muscles, as typically seen with tetanus (see Chapter 25), or, more rarely, with other CNS diseases. However, 'mechanical' abnormalities of the temporomandibular joint (TMJ) (ankylosis due to fracture, luxation, dysplasia, osteoarthritis) or fibrosis of masticatory muscles secondary to chronic masticatory muscle myositis (MMM) may also lead to trismus. Acute-onset MMM, craniomandibular osteopathy, osteomyelitis or tumours affecting the jaw bones or in the vicinity of the TMJ can also lead to severe pain and a reluctance to open the mouth. Dogs are more frequently affected by diseases causing a 'lockjaw' than cats, with the majority of affected dogs being adult.

Neuroanatomical basis

The TMJ of the dog and cat is a transversely elongated condylar synovial joint. The insertion line of the masseter muscle reaches the ventral and rostral aspects of the joint capsule. Medially, the lateral pterygoid muscle, which inserts in the region of the TMJ, supports transverse joint movements and strengthens the joint capsule. The masseter, pterygoid, temporal and digastricus muscles are all innervated by the mandibular branch of the trigeminal nerve (**209**).



▲ **209** **The main muscles of mastication.**

Masticatory muscles contain a unique muscle fibre (type 2M) that differs both histochemically and biochemically from the fibre types present in limb muscles (types 1A and 2A).

The presence of 'lockjaw' can be due to 'genuine' trismus caused by spasm of the jaw muscles or can arise from disease affecting the muscles of mastication or the TMJ itself. Spasms of the jaw muscles reflect a UMN defect, where UMNs or interneurons lose their inhibitory effect on the LMN, which results in increased muscle tone.

With diseases affecting the TMJ or mandible, 'lockjaw' is either due to a mechanical restriction or is pain associated. Moreover, any painful conditions of the skull that cause referred jaw pain can make animals reluctant to open their mouth.

Neurological evaluation

A complete physical and neurological examination is important to distinguish neurological from non-neurological causes of trismus (**210**). Patients should be closely examined for evidence of trauma that could have resulted in TMJ luxation/subluxation. Thorough oral and ophthalmic examinations should be performed. Retrobulbar masses often cause visible swelling or drainage behind the carnassial teeth. Animals with trismus caused by tetanus often show a characteristic facial expression ('risus sardonicus') resulting from an increase in facial muscle tone. With disease affecting the TMJ or mandible itself, the neurological examination will not reveal any deficits, even though masticatory muscles can become severely atrophied over several weeks (disuse atrophy). On an acute basis, there will be no evidence of muscle atrophy. Limb muscle mass, tone and segmental spinal reflexes should be evaluated to investigate the possibility of a more generalized myopathy.

Differential diagnosis

The list of differential diagnoses for trismus is dependent on the overall clinical and neurological evaluation, as well as on signalment, history and course of the disease. The differentials for dogs and cats with trismus are listed in *Table 67*, p. 274.

Specific diagnostic tests for trismus

If trismus is the only presenting sign:

- Type 2M antibody titres in dogs to investigate for MMM.
- CK serum measurement to investigate for a myopathy.
- EMG to exclude a generalized myopathy.
- Muscle biopsy in case of an abnormal EMG.
- Radiographs to assess the TMJ, mandible and bullae.
- Otoscopic examination to assess for middle ear disease causing referred pain and reluctance to open the jaw.
- Advanced diagnostic imaging of the head (CT or MRI) ± CSF tap to exclude other causes of trismus and aid in selection of sites for muscle biopsy.

If additional neurological deficits are present and there is suspicion of structural brain disease:

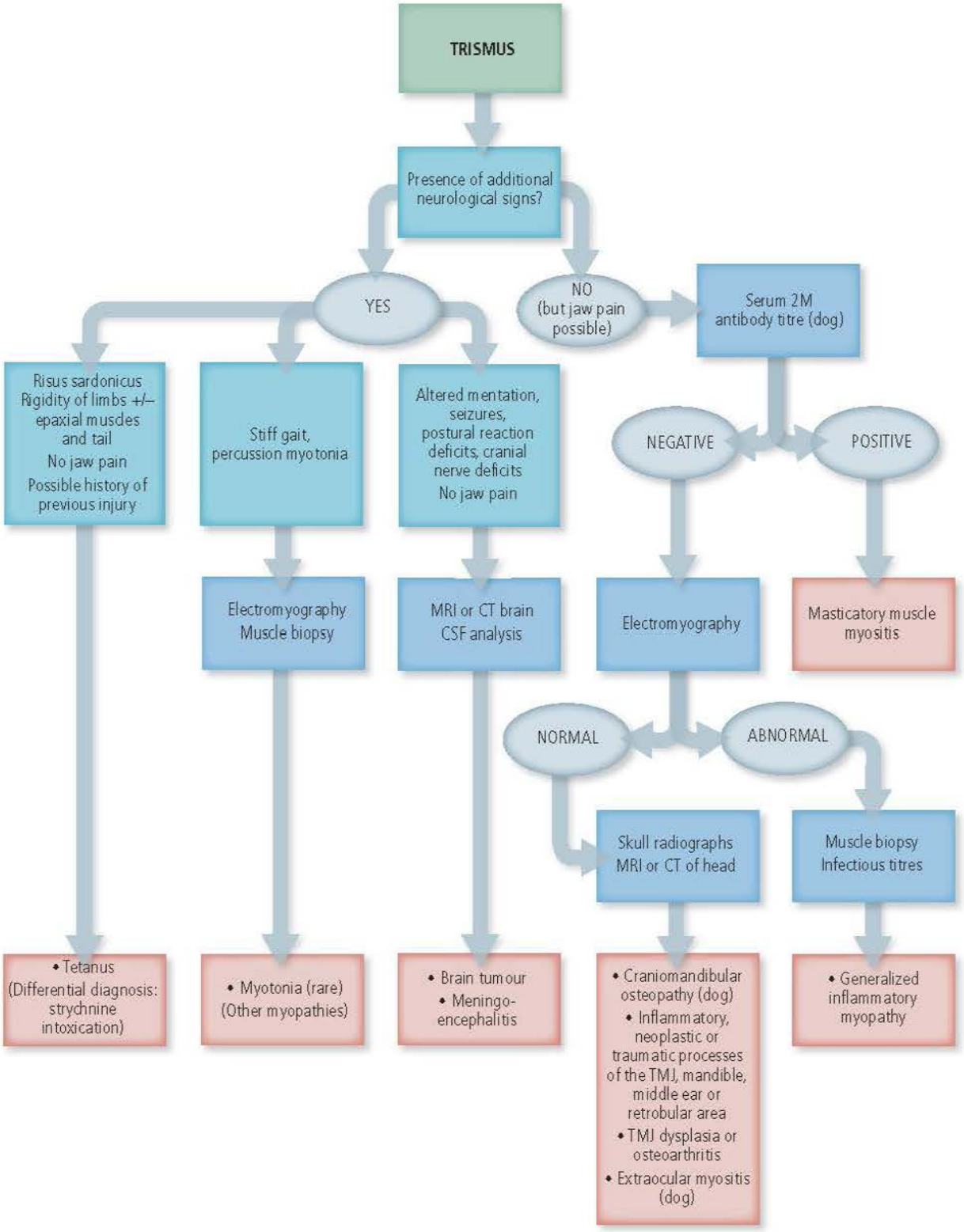
- Advanced brain imaging (CT or MRI).
- CSF analysis (nucleated cell count and cytology, TP concentration); infectious disease titres and PCR as appropriate (see Chapter 19).

If additional signs of a generalized myopathy are present:

- CK serum measurement.
- EMG.
- Infectious titres.
- Muscle biopsy of the masticatory muscles as well as limb muscles.

If myotonic signs are present (e.g. additional muscle stiffness without cramping, muscle dimpling, percussion myotonia after being struck with a reflex hammer):

- EMG – myotonia is characterized by trains of repetitive discharges, which wax and wane in frequency, producing an audible 'dive-bomber' or motorcycle sound. These myotonic discharges are independent of neural control and persist even under GA.
- Genetic tests for myotonia congenita in certain breeds (Miniature Schnauzer, Australian Cattle Dog).
- Exclude hyperadrenocorticism and intoxications (e.g. cholesterol-lowering agents, drugs that block chloride channels) as an underlying cause.



▲ 210 **Diagnostic approach to a patient with trismus.**

Common causes of trismus

Masticatory muscle myositis

Overview

MMM is an autoimmune inflammatory myopathy of the masticatory muscles in dogs. Circulating autoantibodies against masticatory muscle type 2M fibres (fibre type-specific autoantibodies) can be detected in more than 80% of dogs with MMM and are the basis of serological testing for this condition. MMM can be seen in any breed of dog, with no apparent gender predilection. The average age of onset is 3 years. The condition has been reported in dogs as young as 3 months of age (Cavalier King Charles Spaniels).

Clinical presentation

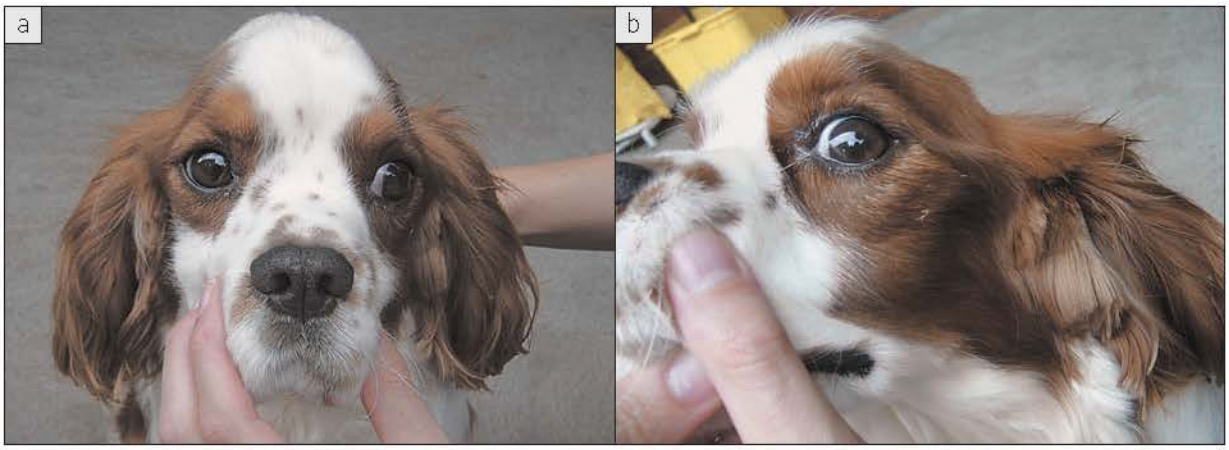
Two types of clinical presentation are seen: the acute painful form and the chronic atrophic form. The acute form presents with bilateral masticatory muscle swelling, occasional ocular signs (exophthalmos, conjunctivitis), pyrexia, mandibular lymphadenopathy and an inability to open the mouth, primarily due to pain. The signs may initially be unilateral without concurrent trismus.

The chronic form is a progression of the acute form and results in marked bilateral masticatory muscle atrophy (**211**). Fibrosis of the muscles can lead to an inability to open the mouth. Forceful opening of the jaw must be avoided, even under sedation or GA.

Table 67 **Causes of trismus**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Masticatory muscle myositis* Inflammatory processes of the TMJ, middle ear or retrobulbar area Meningoencephalitis (rare) Generalized inflammatory myopathies: immune-mediated polymyositis, infectious aetiology (*Toxoplasma*, *Neospora*, *Borrelia*, rickettsial, hepatozoon), para-neoplastic syndrome, breed associated (Newfoundland, Boxer and Hungarian Vizsla) Extraocular myositis (rare)	Inflammatory processes of the TMJ, middle ear or retrobulbar area Meningoencephalitis (rare) Generalized inflammatory myopathies: immune-mediated polymyositis, infectious aetiology (*Toxoplasma*), para-neoplastic syndrome
Trauma	Ankylosis due to fracture or luxation of the TMJ Foreign bodies	Ankylosis due to fracture or luxation of the TMJ Foreign bodies
Toxic	Tetanus* Strychnine	Tetanus* Strychnine
Anomalous	TMJ dysplasia Myotonia congenita (rare)	Myotonia congenita (rare)
Idiopathic	Craniomandibular osteopathy*	
Neoplastic	Tumours of the mandible or TMJ Paraneoplastic polymyositis Brain tumours (rare)	Tumours of the mandible or TMJ Brain tumours (rare)
Degenerative	TMJ osteoarthritis Muscular dystrophy (rare)	TMJ osteoarthritis Muscular dystrophy (rare)

* Common cause



▲ **211** (a) A young Cavalier King Charles Spaniel with bilateral masticatory muscle atrophy due to masticatory myositis. (b) Muscle mass loss associated with masticatory myositis can be profound, revealing underlying bony conformation.

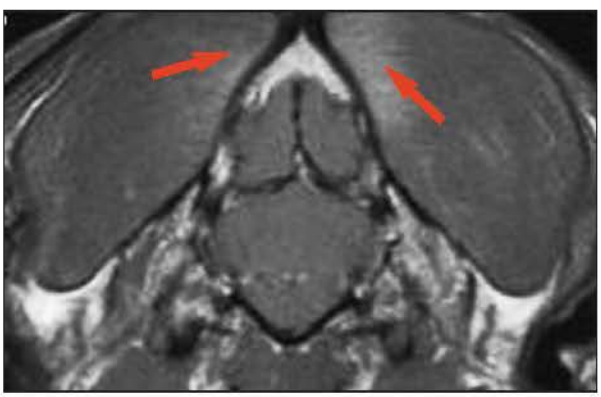
Diagnosis

Diagnosis is based on the presence of serum antibodies against masticatory muscle type 2M fibres. This serum antibody titre is 100% specific, with a sensitivity of 85–90%. Previous corticosteroid medication can result in false-negative results. Some cases of end-stage MMM may also be associated with negative serum results. CK may be elevated in acute stages of the disease.

EMG can help to confirm the selective involvement of masticatory muscles and differentiate MMM from polymyositis. However, EMG may be normal in dogs with end-stage disease because of severe fibrosis and myofibre depletion. Evaluation of muscle biopsy taken from the masticatory muscles can also provide diagnostic confirmation of the disease, as well as provide prognostic information by determining the stage of the disease.

Masticatory muscle biopsies of dogs with MMM are characterized by intense multifocal lymphocytic and plasmacytic perivascular infiltration, occasional eosinophils, and necrosis and phagocytosis of type 2M myofibres.

MRI and CT are mainly helpful for excluding other causes of trismus, but may be an aid in the selection of sites for muscle biopsy (**212**). MRI is not routinely performed to diagnose MMM.



▶ **212** Transverse T1-weighted FLAIR MR image post contrast of the head of a 4-year-old Boxer with masticatory myositis. Note the bilateral hyperintensity within the temporalis muscles secondary to contrast enhancement (arrows). Identification of these areas enabled a more targeted muscle biopsy to be performed, which confirmed the pathology.

Management

Therapy for acute cases consists of immunosuppression with prednisolone (starting at 1–2 mg/kg PO q12h until serum CK and jaw function return to normal, gradually tapering off to the lowest alternate-day dose), which should be maintained for 4–6 months. Serum antibody titres can be used as a treatment guide. Other immunosuppressive agents, such as azathioprine (1–2 mg/kg PO q24h), are indicated in dogs that fail to respond to corticosteroids or that relapse when the dose is tapered.

In chronic cases, prednisolone should be administered at an anti-inflammatory dose for 1 month and physical therapy is recommended. The latter can be performed by encouraging the dog to play with tennis balls or chew rawhide; adequate nutrition is essential at all times.

The prognosis is good if MMM is identified and treated aggressively during the early phase, but persistent muscle atrophy is a common manifestation. (*Note:* Aggressive corticosteroid therapy alone can result in masticatory muscle atrophy, therefore atrophy does not necessarily indicate a progression of the disease.)



◀ **213** Lateral skull radiograph of a 5-month-old West Highland White Terrier that presented with pain on opening the jaw due to craniomandibular osteopathy. Note the osseous proliferation present in the region of the bullae (arrow).

Tetanus

Tetanus should be considered when evaluating any animal with acute onset of head and face abnormalities, especially when trismus is present. Further details can be found in Chapter 25.

Craniomandibular osteopathy

Overview

Craniomandibular osteopathy (CMOP) is a non-neoplastic, developmental bone disease affecting the mandible, tympanic bullae and temporal region of young, growing dogs (4–8 months of age). Lesions are mostly bilateral and consist of irregular enlargement of the affected bones due to cyclical resorption of normal bone and replacement by immature bone. CMOP is inherited in West Highland White Terriers and common in other terrier breeds, but various breeds can be affected. Canine distemper virus and *E.coli* have also been indicated as possible causes.

Clinical presentation

Typical clinical signs include firm swelling of the jaw, difficulty eating, pain on opening the mouth, sometimes an inability to open the mouth, cyclic fever, atrophy of masticatory muscles and lymphadenopathy.

Diagnosis

Diagnosis is usually made via radiographs, which reveal irregular bone thickening (**213**). Rarely, a biopsy is necessary for confirmation.

Management

Pain relief and anti-inflammatory medication (prednisolone) can make the dog more comfortable. Appropriate nutrition needs to be assured. The abnormal bone growth usually ceases by 1 year of age, and lesions may then regress (partially or completely). If the TMJ is severely affected, a permanent inability to move the jaw may result. Surgery may partially correct the problem.

DROPPED JAW

Introduction

'Dropped jaw' is a manifestation of dysfunction (usually bilateral) of the motor component of the trigeminal nerve (LMN disorder). The descriptive terminology for this condition derives from the characteristic clinical presentation (i.e. an inability to close the mouth [mandibular paralysis]). Typically, dogs or cats presenting with dropped jaw also show hypersalivation, with difficulty eating and drinking. Additionally, anorexia, weight loss, lethargy, oral ulceration and masticatory muscle atrophy have been observed. While the cause of the 'dropped jaw' is usually attributed to a motor dysfunction of the trigeminal nerve, some dogs may also present with altered facial sensation (sensory component of the trigeminal nerve), deficits of other CNs (such as the facial nerve) and Horner's syndrome. It is important to remember that an inability to close the mouth can also be due to non-neurological causes. The possibility of mechanical obstruction due to bilateral luxation of the TMJ, fracture of the mandible or oral foreign bodies has to be considered in each patient.

Neuroanatomical basis

The trigeminal nerve (CN V) is the largest CN and has both sensory and motor functions. The mandibular branch contains both motor and sensory fibres. The motor fibres innervate the masseter, temporalis and pterygoid muscles, which are muscles of mastication, as well as the mylohyoid muscle, the rostral belly of the digastricus muscle, the tensor tympani and the tensor veli palatine muscles. The sensory fibres innervate the buccal cavity, tongue, teeth of the lower jaw, skin of the mandible, caudal buccal region and craniolateral pinna. The maxillary and ophthalmic branches contain only sensory fibres. The maxillary branch innervates the lower eyelid, nasal mucosa, upper teeth, upper lip and nose. The ophthalmic branch innervates the medial aspect of the eyelids, the cornea, the nasal mucosa and the skin of the nose. The maxillary and ophthalmic branches also contain post-ganglionic parasympathetic fibres that innervate the lacrimal gland. The sympathetic fibres that supply the pupil also follow the course of the ophthalmic branch.

Neurological evaluation

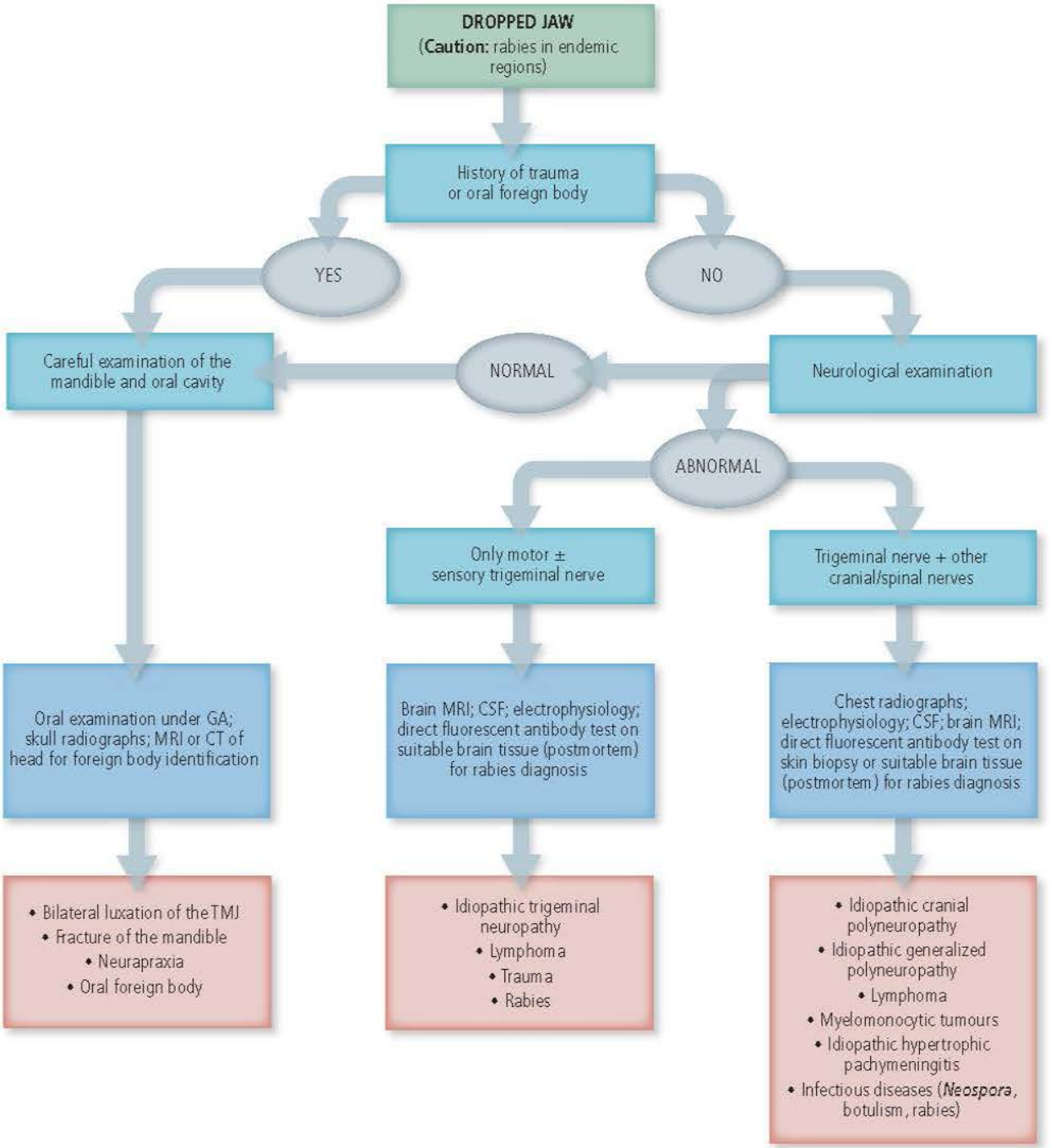
The first step in the evaluation of a patient presenting with dropped jaw is to decide if the cause is neurological (bilateral trigeminal nerve LMN) or non-neurological (mechanical) (**214**, next page).

Non-neurological causes of dropped jaw

- The jaw cannot be closed due to mechanical problems or pain (e.g. TMJ luxation, mandibular fracture, presence of oral foreign bodies).
- Anamnesis (history of trauma), physical examination (presence of pain on manipulation of the jaw), oral cavity inspection and, ultimately, radiographs of the skull should help in the investigation of non-neurological causes of dropped jaw.

Neurological causes of dropped jaw

- Central/brainstem lesion: usually associated with depressed mentation, ataxic/paretic gait and deficits affecting other CNs (e.g. rabies). This is a rare localization.
- Cranial neuropathy: the trigeminal nerve may be the only CN affected or other CNs may also have abnormal function. Generally, mentation and reflexes in all four limbs remain normal.
- Generalized polyneuropathy: trigeminal nerve deficits are accompanied by generalized weakness affecting all four limbs and probably by deficits in other CNs. Mentation should also remain normal.



▲ 214 **Diagnostic approach to a patient with dropped jaw.**

Table 68 **Differential diagnosis of dropped jaw**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Idiopathic hypertrophic pachymeningitis* Rabies Polyradiculoneuritis *Neospora*	Rabies
Trauma	Prehending large, heavy objects (historically reported)	Rare
Toxic	Botulism	Rare
Idiopathic	Idiopathic trigeminal neuropathy* Idiopathic cranial polyneuropathy Idiopathic polyneuropathy	Idiopathic trigeminal neuropathy
Neoplastic	Multicentric lymphoma* Myelomonocytic tumours	Multicentric lymphoma* Myelomonocytic tumours

* Common cause

Differential diagnoses

Disease mechanisms and conditions responsible for acute dropped jaw are listed in *Table 68*.

Specific diagnostic tests for dropped jaw

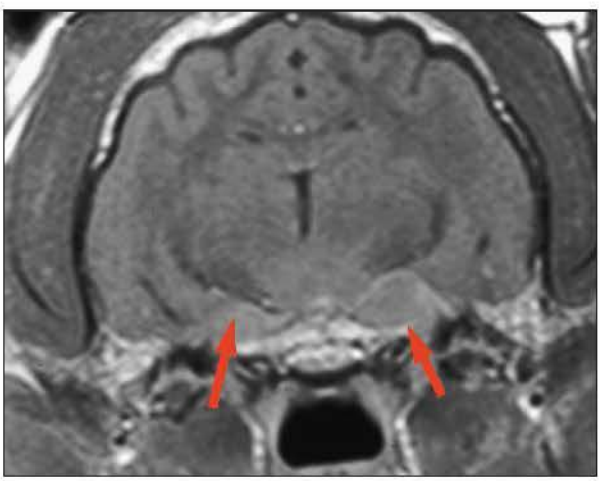
- Thoracic radiographs to evaluate for megaoesophagus in patients with suspected polyneuropathy.
- Sedated examination of larynx to assess for laryngeal paresis in patients with suspected polyneuropathy.
- EMG and motor nerve conduction study are indicated in patients suspected of multiple CN involvement or of a more diffuse polyneuropathy.
- CSF analysis to investigate the possibility of an inflammatory or neoplastic process (lymphoma).
- CT or MRI of the brain to assess for specific CN enlargement and/or contrast enhancement, as well as meningeal thickening and/or contrast enhancement (**215**).

Common causes of dropped jaw

Idiopathic trigeminal neuropathy/neuritis

Overview

Idiopathic trigeminal neuropathy/neuritis (ITN) is the most common benign, neurological cause of sudden inability to close the mouth. It is common in dogs, especially Golden Retrievers, and rare in cats. The aetiology remains unknown. A non-suppurative inflammatory neuritis in the motor branches of the trigeminal nerve and its ganglion has been confirmed in some cases; however, it is unknown whether this inflammatory process occurs in all cases.



▶ **215** **Transverse T1-weighted contrast enhanced MR image depicting bilateral enlargement and hyperintensity of CN V due to lymphoma (arrows).**



▲ 216 A Greyhound with an obvious dropped jaw, which was acute in onset.



▲ 217 A Labrador Retriever with left-sided Horner's and dropped jaw, both of which were sudden in onset.

Clinical presentation

Onset of dropped jaw is usually acute (**216**). Horner's syndrome (**217**), some degree of sensory loss in the sensory distribution of the trigeminal nerve and facial nerve paralysis can occasionally be associated with the dropped jaw. The affected animal struggles to prehend food and water, but retains the ability to swallow.

Diagnosis

ITN is a diagnosis of exclusion and cannot be confirmed antemortem. The only tests that are abnormal in most dogs are EMG and CSF analysis. EMG often reveals positive sharp waves and/or fibrillation potentials in the masticatory muscles unless the dog is tested too soon after the onset of mandibular paralysis (up to 7 days after the onset). CSF analysis is often normal or it can reveal a mild mononuclear pleocytosis, frequently with a normal or mildly elevated protein content.

Management

Treatment is mainly supportive, assisting the animal to eat and drink. Corticosteroid administration appears not to affect the clinical course of the disease. The use of tape muzzles has been recommended to improve ingestion of food, as these dogs are unable to grab food, but can swallow normally. Aspiration pneumonia and dehydration are concerns associated with ineffective supportive care. An oesophagostomy tube can be placed to support nutrition in severely affected animals.

Application of artificial tears or eye lubricants several times daily may be necessary in dogs or cats with evidence of dry eyes to prevent severe corneal injuries and conjunctivitis.

The mean time for recovery ranges from 2–10 weeks. Dogs with a more protracted recovery frequently show marked atrophy of the masticatory muscles caused by prolonged denervation. Dogs with dropped jaw should be encouraged to chew (on natural/synthetic chews). Owners can also be instructed to perform a gentle, passive range of movements of their pet's jaw as part of a physiotherapy plan. The main aim of the physiotherapy is to limit masticatory muscle atrophy and consequent muscle fibrosis.

Idiopathic hypertrophic chronic pachymeningitis

Overview

This condition is a recently recognized cause of multiple CN deficits. 'Dropped jaw' is the most common complaint associated with this condition; however, most dogs also have other CN deficits. Greyhounds and crossbred-sight hounds seem to be predisposed. The condition is characterized by diffuse thickening of the dura mater caused by a fibrosing inflammatory process of the pachymeninges. The aetiology is unknown.

Diagnosis

CSF analysis reveals inflammatory changes in most cases, but can be normal. MRI is key to the diagnosis of this disorder, with thickening, diffuse or localized hyperintensity on T2-weighted and T2-weighted FLAIR images and marked contrast enhancement of the pachymeninges.

Management

Treatment consists of administering immunosuppressive doses of corticosteroids (prednisolone, 1–2 mg/kg PO q12h until remission, followed by tapering dosages). The addition of other immunosuppressants, such as cytosine arabinoside, seems to help achieve a better control of the disease. Although most dogs achieve clinical remission, a cure is more difficult to obtain.

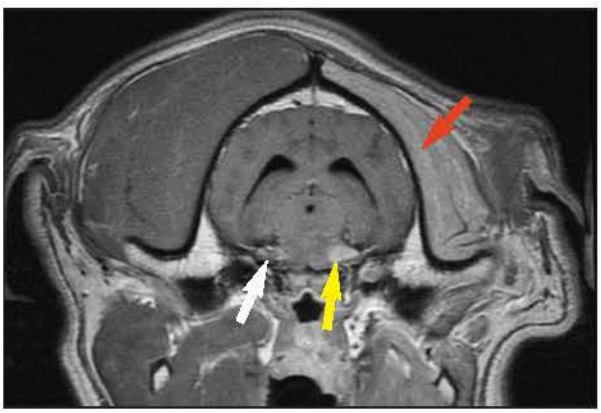
MASTICATORY MUSCLE ATROPHY

Introduction

Masticatory muscle atrophy can occur unilaterally or bilaterally. It can result from impaired innervation due to lesions of the motor branch of the trigeminal nerve, lesions affecting the masticatory muscles themselves or systemic disorders. Systemic disorder is not often a cause of unilateral muscle atrophy.

Unilateral masticatory muscle atrophy

- Due to muscle disorders:
  - Unilateral masticatory muscle atrophy is uncommon with myositis and, when present, a trigeminal nerve disorder should be suspected. However, acute presentations should prompt consideration of a muscle disease.
- Due to unilateral trigeminal nerve disorders:
  - Unilateral involvement of the motor part of CN V causes ipsilateral masticatory muscle atrophy secondary to neurogenic atrophy and decreased jaw tone.
  - Enophthalmia and protrusion of the third eyelid can be observed in the ipsilateral eye (passive retraction of the eyeball secondary to loss of temporalis and digastricus muscle mass). Decreased or complete loss of facial sensation may be seen with associated involvement of trigeminal sensory nerve branches. Involvement of the ophthalmic branch of CN V can also result in decreased tear secretion and neurotropic keratitis secondary to the loss of the afferent portion of the lacrimal reflex. Other neurological signs (e.g. hemiparesis, facial nerve paralysis, circling, mydriasis) may be seen as the result of expansion of a mass lesion within the cranial cavity and subsequent damage to adjacent brainstem structures.
- Underlying causes for this unilateral CN V dysfunction commonly include trigeminal nerve sheath tumours and neuritis. In comparison to nerve sheath tumours, inflammatory diseases restricted to individual cranial nerves are uncommon in dogs. Possible causes of cranial neuritis include autoimmune and infectious processes.
- MRI allows an earlier diagnosis of these trigeminal nerve lesions, but it must be remembered that this specific CN will normally enhance following paramagnetic contrast administration due to its associated vascularity (**218**).



▲ **218** **Transverse T1-weighted, contrast-enhanced MR image of a dog with masticatory muscle atrophy (red arrow) due to an ipsilateral nerve sheath tumour of CN V (yellow arrow). Note the contralateral normal CN V is usually hyperintense secondary to contrast enhancement (white arrow).**



▲ **219** **A Dachshund with bilateral masticatory muscle atrophy due to chronic steroid administration.**

Bilateral masticatory muscle atrophy

Bilateral masticatory muscle atrophy can be caused by the following diseases:

- Bilateral involvement of the motor branches of CN V (see Dropped jaw, above), which is usually associated with reduced jaw tone, a dropped jaw and/or an inability to close the mouth voluntarily.
- Systemic disorders (cachexia, hyperadrenocorticism or exogenous steroid administration) (**219**).
- Chronic MMM. In cases of chronic MMM, the atrophy is caused by destruction of myofibres and fibrotic scarring. It is usually associated with a reduced ability to open the jaw (see Trismus, above).
- Idiopathic condition – poorly documented.

As with unilateral atrophy, bilateral masticatory muscle atrophy may cause enophthalmia and protrusion of the third eyelid.

FACIAL PARALYSIS

Introduction

Facial paresis or paralysis is often featured as a sole sign, as seen with idiopathic facial paresis/paralysis. However, it can also occur with more complex diseases of the middle/inner ear or CNS, and can occasionally reflect part of a generalized peripheral neuropathy. Muscles that regulate facial expression and maintain a physiological appearance of the mouth, ear position and palpebral fissure are innervated by the facial nerve (CN VII). A thorough neurological examination will help to localize the problem, establish an appropriate list of differential diagnoses and determine the choice of diagnostic tests.

Neuroanatomical basis

The facial nerve is motor to the muscles of facial expression and sensory (providing the sense of taste) to the rostral two-thirds of the tongue and hard palate. Its parasympathetic component innervates the lacrimal gland and the mandibular and sublingual salivary glands. Neurons innervating the muscles of facial expression are located in the facial nucleus in the rostral medulla oblongata. The axons pass in the internal acoustic meatus of the petrosal bone on the dorsal surface of the vestibulocochlear nerve and leave the skull through the stylomastoid foramen. The facial nerve courses through the middle ear before branches are distributed to the muscles of facial expression (ear, eyelids, nose, cheeks and lips) as well as the caudal portion of the digastricus muscle (**220**).

Motor dysfunction of CN VII produces the following signs: drooping and inability to move the ear and lip, drooling, widened palpebral fissure, absent spontaneous and provoked blinking, absent abduction of the nostril during inspiration and deviation of the nose towards the normal side due to the unopposed muscle tone on the unaffected side (**221**). With chronic denervation, the lips are retracted further than normal and the nostril is deviated to the affected side as a result of muscle fibrosis. Lesions of the individual branches of the facial nerve produce paresis or paralysis of the specific muscle they innervate. Involvement of the parasympathetic supply of the lacrimal and nasal glands produces keratoconjunctivitis sicca and a dry nose (**222**), respectively.

Neurological evaluation

The neurological evaluation should help to localize the problem as a central CN disease or a peripheral CN disease (**223**, next page):

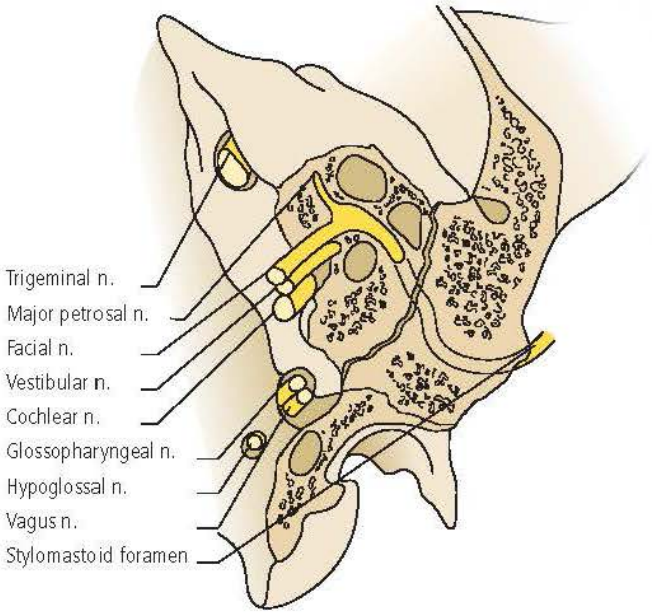
- **Central cranial nerve disease/brainstem disorder causing facial paralysis.** If the brainstem is affected, hemiparesis and/or postural reaction deficits are usually present. These occur on the same side as the facial paresis/paralysis. Moreover, brainstem signs can include the involvement of further CNs, altered mentation or presence of vestibulocerebellar signs.



▲ 221 **A Boxer with acute-onset left-sided facial paresis.**



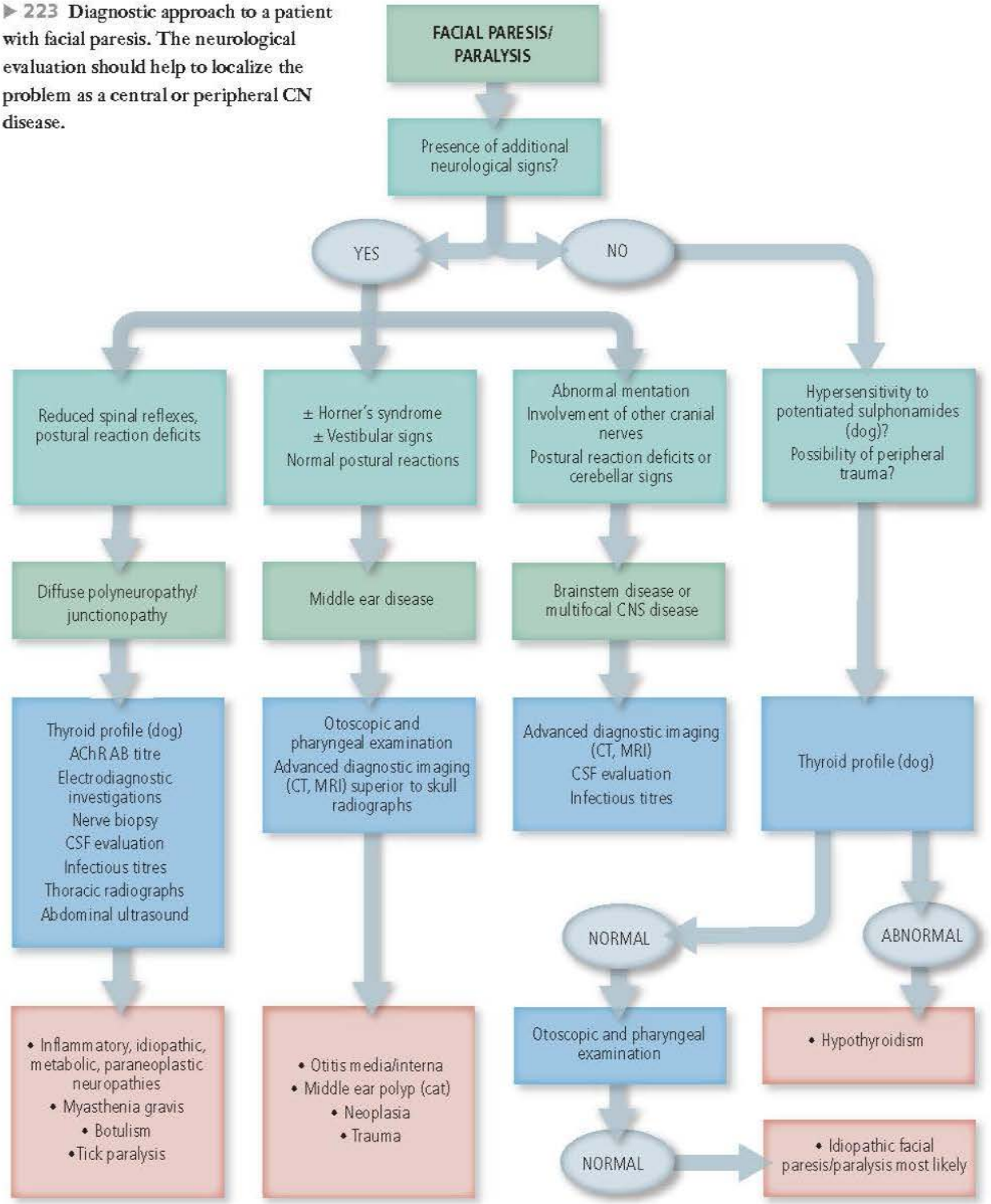
▲ 222 **Some patients with facial nerve dysfunction can present with an ipsilateral dry nose.**



▲ 220 **The intracranial anatomical course of the facial nerve once it has left the brainstem.**

- **Peripheral nerve disease causing facial paralysis:**
  - Middle/inner ear disease. If there is evidence of ipsilateral vestibular signs (see Chapter 14) and/or Horner's syndrome without any postural reaction deficits, a middle/inner ear neurolocalization must be suspected based on the close proximity of CN VIII and the cranial cervical ganglion/post-ganglionic sympathetic neurons.
  - Polyneuropathy. If spinal reflexes are reduced, the facial paresis/paralysis may be part of a more generalized peripheral neuropathy (see Chapter 10). Facial weakness, in particular a decrementing blink reflex, may be seen with junctionopathies, such as MG, or, more rarely, botulism (see Chapters 24 and 25, respectively) and tick paralysis, especially in Australia.
  - Idiopathic facial nerve dysfunction. If facial paresis/paralysis occurs as the sole sign, idiopathic facial paresis is the most likely diagnosis. However, even though hypothyroidism commonly causes polyneuropathies, facial paresis may be the only clinical sign.

▶ **223** **Diagnostic approach to a patient with facial paresis. The neurological evaluation should help to localize the problem as a central or peripheral CN disease.**



Differential diagnosis

Disease mechanisms and conditions responsible for facial paralysis/paresis are listed in *Table 69*.

Facial muscle weakness can be seen in conjunction with MG, botulism or tick paralysis; facial paresis/paralysis (often bilateral, but may be asymmetrical) may theoretically occur as part of any acute-onset peripheral neuropathy; however, more generalized neuropathic signs should also be present.

Specific diagnostic tests for facial paresis

If facial paresis/paralysis is the only presenting sign:

- Thyroid function testing (dog): total T4 and TSH determinations as minimum screening; if inconclusive, free T4, T3 and antithyroid antibody levels should be analysed.
- Otoscopic and pharyngeal examination (particularly to check for possible inflammatory polyps in cats) should be performed under GA if necessary.
- If otitis media/interna is suspected from the history, see below.

Table 69 **Causes of facial paresis/paralysis**

DISEASE MECHANISM	DOGS	CATS
Vascular	Brain haemorrhage/infarct (rare cause)	Brain haemorrhage/infarct (rare cause)
Inflammatory/infectious	Otitis media/interna* Meningoencephalitis of unknown aetiology (e.g. GME) Infectious encephalitis (distemper, rabies, *Toxoplasma, Neospora*, fungal, bacterial, rickettsial) Acute canine polyradiculoneuritis (Chronic demyelinating polyradiculoneuritis)	Otitis media/interna* Middle ear polyps Meningoencephalitis of unknown aetiology (presumed immune mediated) (rare) Infectious encephalitis (*Toxoplasma*, FIP, rabies, bacterial, fungal)
Trauma	Head trauma/peripheral facial trauma Iatrogenic following bulla osteotomy	Head trauma/peripheral facial trauma Iatrogenic following bulla osteotomy
Toxic	Hypersensitivity associated with potentiated sulphonamides Tick paralysis (see Chapter 10)	Tick paralysis
Anomalous	Chiari-like malformation (mild facial paresis, possibly bilateral)**	
Metabolic	Hypothyroidism*	
Idiopathic	Idiopathic facial nerve paresis/paralysis* Acquired myasthenia gravis*	Idiopathic facial nerve paresis/paralysis Acquired myasthenia gravis
Neoplastic	Primary or metastatic brain tumour Middle ear tumour	Primary or metastatic brain tumour Middle ear tumour

* Common cause

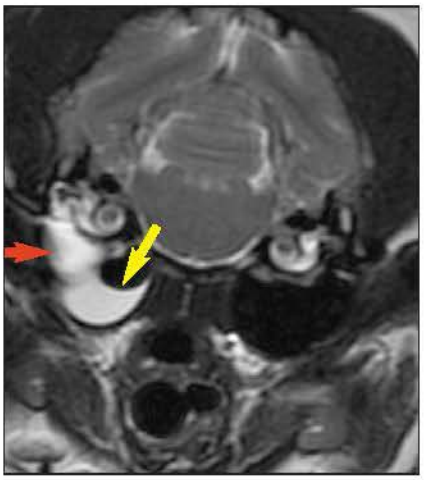
** If Chiari-like malformation is associated with syringomyelia, neck/flank scratching, neck pain and postural reaction deficits due to the latter are the most common signs.

If otitis media/ interna is suspected (history, concurrent vestibular signs and/or Horner's syndrome):

- Otoscopic and pharyngeal examination should be performed, if necessary under GA.
- Swabs for cytology and culture (aerobic, fungal and yeast) from the middle ear cavity if the tympanic membrane is ruptured.
- Myringotomy with a 20-gauge spinal needle to obtain samples from the middle ear cavity for cytology and culture if the tympanic membrane is intact, but bulging, or of an abnormal colour.
- Imaging of the tympanic bullae with radiographs, CT or MRI to assess for otitis media/interna (**224**).

If CNS involvement is suspected (postural reaction deficits, altered mental status, other CN deficits, cerebellar or forebrain signs):

- Advanced brain imaging (CT or MRI).
- CSF analysis (nucleated cell count and cytology, TP concentration).
- Serum and CSF infectious disease titres and/or PCR for various infectious organisms, and CSF culture if indicated.



▲ **224** Transverse T2-weighted MR image at the level of the tympanic bullae of a cat with otitis media. Fluid accumulation can be noted in both the ventromedial (yellow arrow) and dorsolateral (red arrow) compartments of the feline bulla.

If a polyneuropathy or more generalized neuromuscular disease is suspected (reduced spinal reflexes, postural reaction deficits, other CN involvement):

- EMG and motor nerve conduction studies are indicated in patients suspected of a more diffuse polyneuropathy or multiple CN neuropathy.
- Search for an attached tick.
- Consider botulism intoxication.
- Thyroid function testing (dog).
- If electrodiagnostic testing is abnormal: chest radiographs and abdominal ultrasound to exclude paraneoplastic polyneuropathy; muscle and nerve biopsy may aid in definitive diagnosis.
- Anti-AChR antibody titre to rule out focal MG in cases showing facial paresis.
- CSF analysis (nucleated cell count and cytology, TP concentration).
- Serum and CSF infectious disease titres and/or PCR for various infectious organisms, and CSF culture if indicated.

Common causes of facial paresis/paralysis

Idiopathic facial nerve paresis/paralysis

Overview

Most common cause of facial nerve paresis/paralysis in dogs and cats. Cocker Spaniels and Boxers are predisposed. The aetiology is unknown.

Clinical presentation

Occurs mostly as unilateral dysfunction, but may occur bilaterally. Other neurological deficits are usually absent, although some animals might develop concurrent idiopathic vestibular syndrome.

Diagnosis

Diagnosis is made by exclusion of other possible causes. Even in the absence of other neurological deficits, a thorough investigation for ear disease, as well as blood tests for hypothyroidism (dog), is recommended. CSF evaluation can help exclude CNS inflammatory causes of facial paresis. MRI revealing lack of contrast enhancement of the intratemporal part of the facial nerve may be associated with a better outcome in dogs with idiopathic facial paralysis.

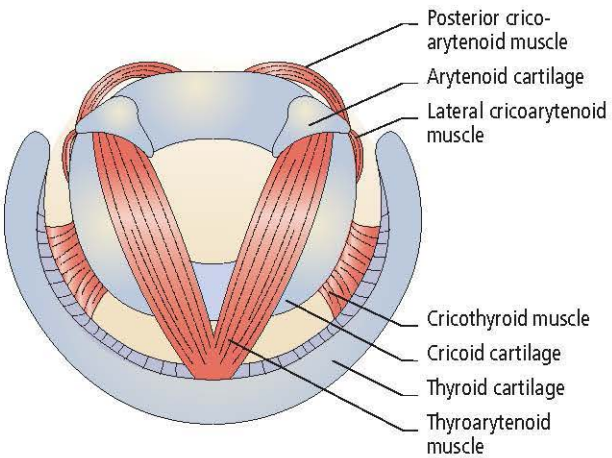
Management

No specific treatment exists. Even though tear production is expected to be normal with idiopathic facial paresis/paralysis, corneal lesions may occur because of exposure due to reduced eyelid closure, and this should be addressed. The prognosis for complete recovery is guarded; recovery can take weeks to months, but may not occur at all. Occasionally, this disorder progresses to affect both facial nerves. Chronicity may result in muscle contracture and deform the facial expression permanently.

STRIDOR AND DYSPHONIA

Introduction

Respiratory stridor and/or dysphonia are characteristic signs of laryngeal dysfunction (paresis or paralysis). Laryngeal paralysis is an important cause of upper respiratory airway obstruction in dogs and it is increasingly being recognized in cats. Clinical signs of laryngeal paralysis in dogs typically include stridor, exercise intolerance, respiratory distress, dysphonia, cyanosis, cough and collapse. Cats manifest similar clinical signs, but can also show tachypnea, dysphagia, weight loss, anorexia and fever. The age of dogs presenting with laryngeal paralysis has a bimodal distribution, with immature or young dogs usually less than 1 year of age and older dogs (mean age ranging from 9.5–12.2 years) being most affected. Both inherited and acquired diseases are recognized. Young dogs usually suffer from inherited laryngeal paralysis, while older animals may have the acquired form of this disease.



◀ **225 Anatomy in cross section of the laryngeal muscles.**

Inherited laryngeal paresis

The hereditary form of laryngeal paresis/paralysis has been described in many different breeds including Bouvier des Flandres, Siberian Huskies, white-coated German Shepherd Dogs, Dalmatians, Rottweilers, Leonbergers, Bull Terriers and Pyrenean Mountain Dogs. Laryngeal paresis/paralysis has also been reported in a young Afghan Hound, Cocker Spaniel, Dachshund and Miniature Pinscher. In some of these breeds (Bouvier des Flandres, Dalmatians, Rottweilers, Leonbergers and Pyrenean Mountain Dogs) laryngeal paralysis is part of a more generalized NM disorder that is referred to as laryngeal paralysis/polyneuropathy complex.

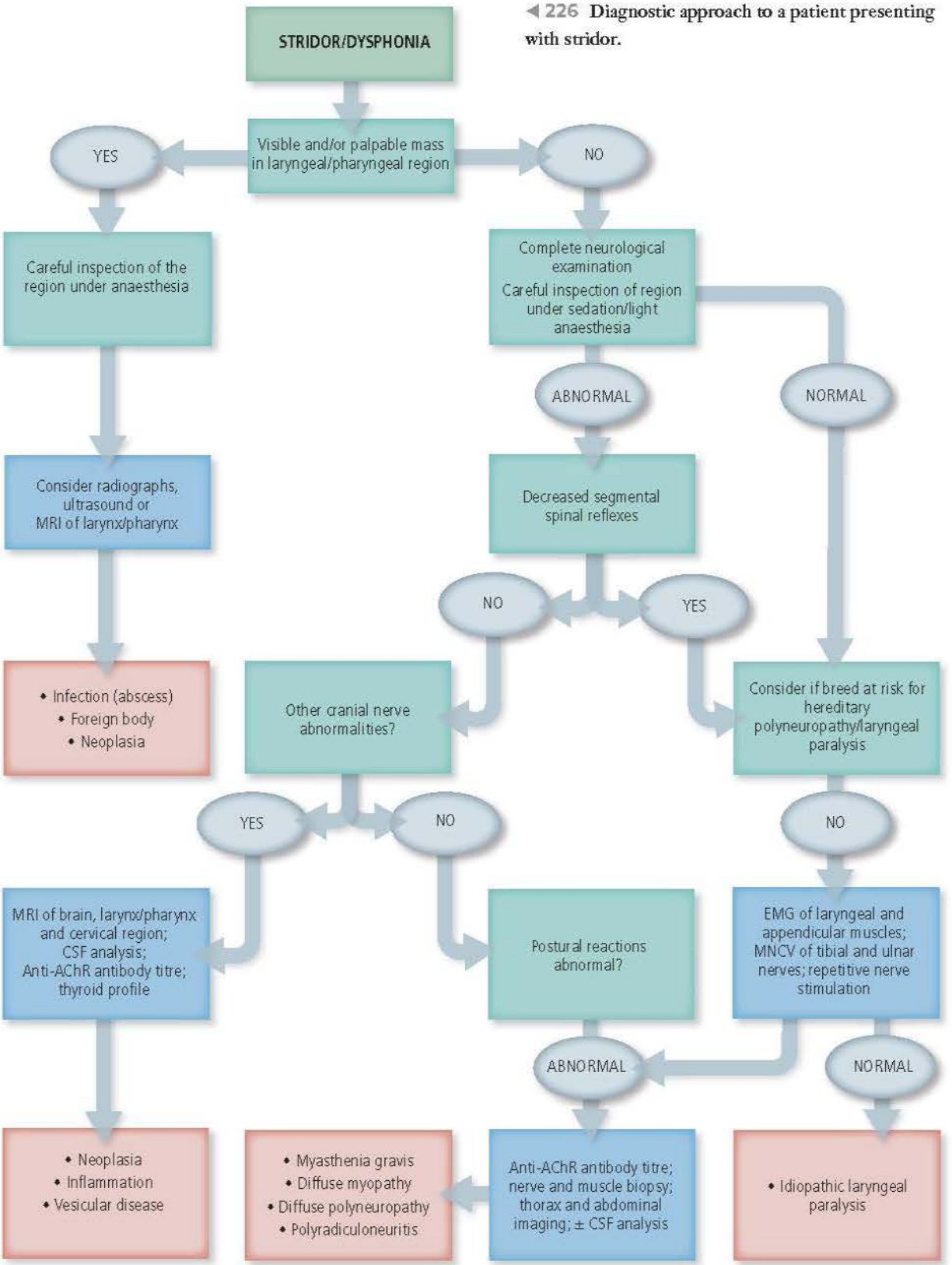
Acquired laryngeal paresis

Acquired laryngeal paralysis seems to affect mainly older, large/giant breed dogs with Labrador Retrievers being overrepresented. Some reports found male dogs more affected than females (3.7:1). The cause of this acquired form is most often described as idiopathic. Other causes include thyroid neoplasia, surgical trauma to the vagus nerve and inflammatory or neoplastic brainstem diseases. Laryngeal paralysis has also been described in association with more generalized NM disorders such as MG and acquired polyneuropathies. Hypothyroidism has also been implicated as a cause , but the relationship between these two conditions is still unclear. Laryngeal paralysis in cats does not seem to have any sex or breed predisposition. The median age of cats reported with laryngeal paralysis is 11 years, with a very broad range from 4 months to 17 years of age.

Neuroanatomical basis

The larynx is a very complex structure that is controlled by both intrinsic and extrinsic muscles (**225**). Innervation of three of the four intrinsic laryngeal muscles is supplied by the recurrent laryngeal nerve (dorsal and lateral cricoarytenoid muscle and thyroarytenoid muscle). The fourth muscle (cricothyroid muscle) is supplied by the cranial laryngeal nerve. Both the recurrent laryngeal nerve and the cranial laryngeal nerve originate from the vagus nerve. The cranial laryngeal nerve leaves the vagus nerve at the level of the distal ganglion (ventral and

◀ 226 **Diagnostic approach to a patient presenting with stridor.**



medial to the tympanic bulla), while the vagus nerve gives rise to the recurrent laryngeal nerve at the level of the thoracic inlet. The cell bodies of these somatic efferent fibres are located in the nucleus ambiguus in the medulla oblongata.

Neurological evaluation

The neurological examination should aim to identify non-neurological causes of stridor/dysphonia and other neurological deficits (**226**). This may help to differentiate between peripheral CN disease (NM) versus central CN disease (brainstem).

Non-neurological causes of stridor/dysphonia

- Laryngeal trauma (foreign body).
- Mass effect on the larynx (neoplastic lesion, abscesses or granulomatous lesions).
- Local inflammatory/infiltrative processes (laryngitis, polyps).

In the above scenario the neurological examination should be completely normal and inspection of the larynx under sedation/light anaesthesia should reveal normal laryngeal function or restricted movement due to mass effect on this structure. Occasionally, external palpation of the larynx may identify a mass lesion at this level with or without associated discomfort.

Neurological causes of stridor/dysphonia

- Central/brainstem lesion: usually associated with other neurological signs such as depressed mentation, ataxic/paretic gait and deficits affecting other CNs.
- Cranial polyneuropathy: other CNs may have abnormal function. Generally, mentation, gait and segmental spinal reflexes in all four limbs remain normal.
- Part of a generalized polyneuropathy: dysphonia is accompanied by generalized weakness affecting all four limbs and probably by deficits in other CNs. Mentation should remain normal.

Differential diagnosis

The list of differential diagnoses in dogs or cats that present with stridor/dysphonia varies enormously depending on the signalment and history, as well as the physical and neurological examination findings. Disease mechanisms and conditions commonly associated with the emergency evaluation of a dog or a cat with stridor or dysphonia are outlined in *Table 70* (next page).

Specific diagnostic tests for stridor/dysphonia

Electrophysiological tests, such as EMG, MNCV evaluation and repetitive motor nerve stimulations, should be performed in every patient presenting with laryngeal paralysis to investigate the possibility of a generalized NM disorder. Intrinsic laryngeal muscles as well as axial and appendicular muscles should be thoroughly evaluated with EMG, and MNCV studies should be performed on both the tibial and ulnar nerves. These electrophysiological tests are invaluable for investigating concomitant or underlying NM disorders such as polyradiculoneuropathies, polymyopathies or MG. If a generalized NM disorder is identified, further diagnostic tests (endocrine testing, anti-AChR antibody titre, muscle and nerve biopsy, thorax and abdominal imaging, ± CSF analysis) should be carried out to identify a specific cause.

Common causes of stridor/dysphonia

Idiopathic laryngeal paralysis

Overview

Idiopathic laryngeal paralysis affects mostly middle-aged and older large or giant breeds dogs such as Labrador Retrievers, Chesapeake Bay Retrievers, Irish Setters, Afghan Hounds, St Bernards and Rottweilers. Sporadically, medium and small/toy breeds can be affected. Laryngeal paralysis classically results from unilateral or, more commonly, bilateral denervation of the laryngeal abductor muscles (dorsal cricoarytenoid).

Table 70 **Differential diagnosis of stridor/dysphonia**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Meningoencephalitis of unknown origin Rabies Trypanosomiasis (rare)	Meningoencephalitis of unknown origin (rare) Rabies
Trauma	Cervical/thoracic traumas Iatrogenic after cervical/thoracic surgery Iatrogenic after aggressive attempts at external jugular venipuncture	Cervical/thoracic traumas Iatrogenic after cervical/thoracic surgery Iatrogenic after aggressive attempts at external jugular venipuncture
Toxic		Lead poisoning
Metabolic	Hypothyroid polyneuropathy	
Idiopathic	Idiopathic laryngeal paralysis* Polyradiculoneuritis* Acquired myasthenia gravis	Idiopathic laryngeal paralysis* Polyradiculoneuritis* Acquired myasthenia gravis
Neoplastic	Mass effect on laryngeal nerves	Mass effect on laryngeal nerves Lymphoma
Degenerative	Hereditary laryngeal paralysis (breed specific)	

* Common cause

Diagnosis

Diagnosis is based on clinical examination, laryngoscopy showing impaired abduction of the larynx and EMG evidence of denervation potentials in the intrinsic laryngeal muscles. EMG is also helpful in detecting more generalized LMN disorders. Motor nerve conduction velocity studies of the recurrent laryngeal nerve can be performed to more specifically define the origin of the EMG abnormalities (neuropathy versus myopathy).

Management

While conservative treatment of laryngeal paralysis is generally ineffective in halting the disease progression, it may help prevent acute exacerbation of the clinical signs (cyanosis and collapse). Guidelines for the conservative management of laryngeal paralysis include exercise restriction, avoiding stressful situations and encouraging owners to keep their dog/cat lean and not overweight.

A variety of surgical techniques have been successfully used for the treatment of laryngeal paresis/paralysis; these include ventriculocordectomy, partial arytenoidectomy, laryngeal tieback, modified castellated laryngofissure and neuromuscular pedicle grafting. Of all these techniques, arytenoid tieback surgery appears to give the best overall results.

Idiopathic laryngeal paralysis in older dogs can have a favourable prognosis if appropriately treated. In dogs that have concurrent conditions, such as megaoesophagus, the prognosis is generally poor.

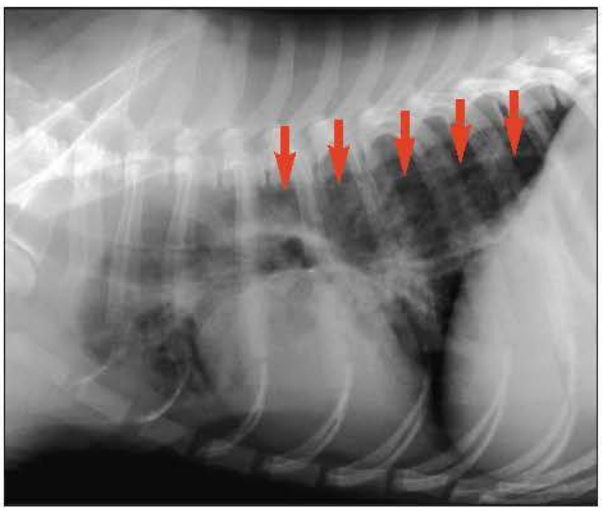
DYSPHAGIA AND REGURGITATION

Introduction

Dysphagia is defined as difficulty in swallowing. Regurgitation refers to emitting already swallowed food or drink and should be distinguished from vomiting; it is mostly associated with megaoesophagus (**227**), which describes a dilation of the oesophagus.

Dysphagia and regurgitation can result from functional or morphological abnormalities of the oropharyngeal area or oesophagus. They can occur as a sole sign or be part of a more complex disease of neurological/NM origin. In some NM diseases, such as MG, dysphagia and regurgitation may be the only clinical signs.

Dysphagia and regurgitation often compromise nutrition and hydration and may lead to aspiration pneumonia and dehydration. It is therefore important to recognize these signs early and to try to establish the underlying cause as soon as possible to initiate appropriate treatment.



▲ **227** Lateral thoracic radiograph of a dog with megaoesophagus. The dorsal border of the dilated oesophagus is clearly visible (arrows).

Neuroanatomical basis

Normal swallowing and dysphagia

Normal swallowing relies on a very complex, well-coordinated function between the tongue, hard and soft palates, pharynx, oesophagus and gastro-oesophageal junction. It is coordinated by CNs V (trigeminal; motor innervation of masticatory, mylohyoid and soft palate muscles; sensory fibres from oral cavity), VII (facial; motor innervation of stylo- and jugulohyoid muscles; sensory fibres from soft palate and nasopharynx), IX (glossopharyngeal; motor fibres to pharyngeal muscles; sensory fibres from pharynx and tongue), X (vagus; motor fibres to pharyngeal muscles and oesophagus; sensory fibres from pharynx, tongue and oesophagus) and XII (hypoglossal; motor fibres to tongue) and their nuclei in the brainstem, which in turn are controlled by areas of the reticular formation referred to as the swallowing centre.

Swallowing disorders (dysphagias) can arise from functional or morphological abnormalities of any of the structures involved. They may be classified as:

- **Oropharyngeal dysphagia** (impaired bolus formation or passage from the mouth to the cranial oesophagus).
- **Oesophageal dysphagia** (impaired bolus passage from the cranial oesophagus to the gastro-oesophageal junction).
- **Gastro-oesophageal dysphagia** (disturbance in the passage from the oesophagus into the stomach).

The oropharyngeal phase of swallowing can be further subdivided into oral, pharyngeal and cricopharyngeal stages:

- **Oral dysphagia** is associated with disorders of initiation of swallowing (bolus accumulation at the base of the tongue).
- **Pharyngeal dysphagia** describes a disorder in propulsion of the bolus across the pharynx (rostral to caudal pharyngeal contractions propel the bolus from the base of the tongue to the cricopharyngeal passage).
- **Cricopharyngeal dysphagia** describes failure of relaxation (achalasia) or closure (chalasia) of the cricopharyngeal sphincter and lack of coordination of sphincter relaxation with pharyngeal or oesophageal contraction.

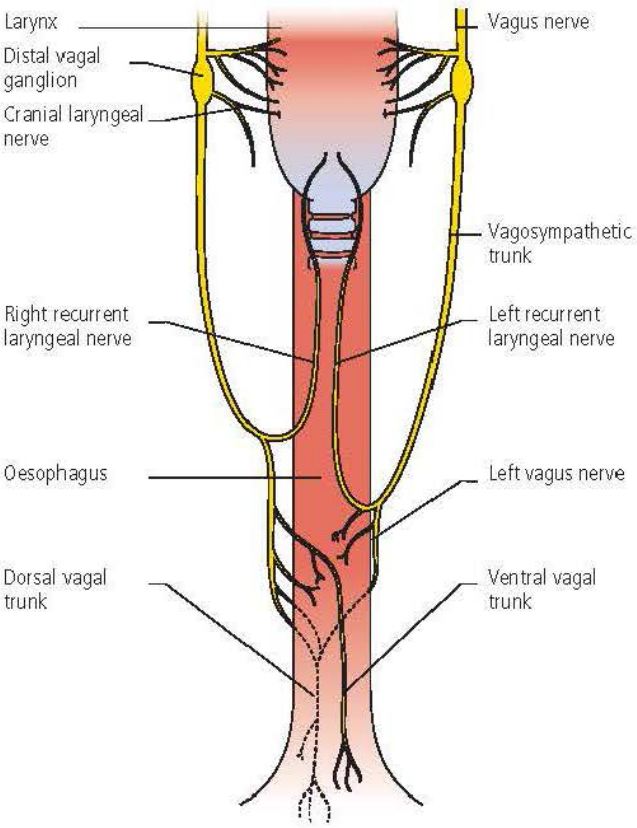
In this section, dysphagia will refer to disorders affecting the pharyngeal and cricopharyngeal phases of swallowing. Disease causing oesophageal and gastro-oesophageal dysfunction will be listed under Regurgitation and megaoesophagus, below.

An intact gag reflex (pharyngeal reflex) is a prerequisite for intact swallowing. The gag reflex is elicited by the glossopharyngeal and vagal nerves, which both arise from the caudal brainstem where they share their sensory (solitary nucleus) and motor (nucleus ambiguus) nuclei. Therefore, lesions of the caudal brainstem, or CNs IX and X themselves, can result in reduced pharyngeal tone and dysphagia. However, more generalized neuropathies must not be overlooked.

Disorders of NM transmission are frequently associated with dysphagia and reduced pharyngeal tone. Dysphagia can also occur due to disease that leads to spasms of the pharyngeal musculature, such as tetanus (Chapter 25). Furthermore, dysphagia is a common clinical sign of generalized myopathies (Chapter 8), in particular those of inflammatory origin. With dystrophin deficient muscular dystrophy, hypertrophy of the pharyngeal muscles may be pronounced and lead to marked dysphagia.

Simple physical obstructions in the head and neck area, such as foreign bodies or neoplastic masses, may be the underlying cause of dysphagia. Animals with pharyngitis or tonsillitis may have difficulty swallowing as well.

In some cases, no underlying cause for dysfunction of the swallowing reflex can be found (idiopathic dysphagia). If the cricopharyngeal muscle fails to open during swallowing, the condition is also called cricopharyngeal achalasia, which predominantly occurs as an idiopathic disease in young dogs.



▲ **228 Anatomical representation of the vagus nerve.**

Regurgitation/megaoesophagus

Regurgitation is the result of oesophageal motility dysfunction or is due to structural abnormalities. It may or may not be associated with overt megaoesophagus. Megaoesophagus occurs more commonly in dogs than in cats.

The oesophagus is innervated by the vagus nerve (**228**). The cervical part is innervated by the pharyngeal and recurrent laryngeal branches and the thoracic portion is innervated by vagal branches. In addition, CN XI (spinal accessory nerve) sends a few fibres to join the vagus nerve. The oesophagus of the dog consists entirely of striated muscle, whereas in the cat the distal third is composed of smooth muscle.

Megaoesophagus can be congenital or acquired and may be primary/idiopathic or occur secondarily to a number of causes. Underlying causes of congenital megaoesophagus include congenital idiopathic megaoesophagus, megaoesophagus as a consequence of a persistent right aortic arch or as an aspect of congenital MG (Chapter 24). Recent studies suggest that the main underlying cause of congenital idiopathic megaoesophagus is a selective rather than an afferent dysfunction of the vagus nerve. Acquired megaoesophagus can be seen with brainstem disease or be a sign of a more generalized polyneuropathy or myopathy, especially the generalized inflammatory myopathies. Megaoesophagus is frequently seen with junctionopathies and occurs in 80% of dogs with acquired MG. Regurgitation may be the sole sign or

it may be associated with generalized weakness. The incidence of oesophageal dilation in cats with acquired MG is lower. Moreover, feline and canine dysautonomia is frequently associated with megaoesophagus and regurgitation. In dogs, megaoesophagus has also been associated with metabolic diseases, such as hypothyroidism and Addison's disease, or with systemic lupus erythematosus.

Apart from functional causes, structural abnormalities such as tumours in the neck or chest area, foreign bodies or oesophagitis with possible secondary strictures may be underlying causes of megaoesophagus and regurgitation. However, in many cases of acquired megaoesophagus or dysmotility of the oesophagus, the underlying cause remains unclear (acquired idiopathic megaoesophagus or dysmotility).

Neurological evaluation

A full clinical and neurological evaluation is important to decide whether dysphagia and/or regurgitation results from a functional disorder or a structural abnormality and occurs as the sole clinical sign or as part of a more complex disease involving the NM, central or autonomic nervous system (**229**, next page). In addition, prehension disorders must be distinguished from dysphagia and regurgitation must be distinguished from vomiting.

Assessment of a functional versus a structural disorder

If the cause of dysphagia or regurgitation is structural or mechanical (e.g. tumour or foreign body, stricture due to inflammatory processes, regurgitation due to persistent right aortic arch), the neurological examination will be unremarkable.

In the case of functional dysphagia, the pharyngeal tone will mostly be decreased and the gag reflex will be weak or absent. However, dysphagia can also be due to spasms of the pharyngeal muscles (tetanus, myotonia). The gag reflex can be tested by applying external pressure to the hyoid bones or by stimulating the pharynx directly with a finger. Alternatively, pharyngeal function can be indirectly assessed by observing the animal eat or drink or by opening its mouth wide, which is normally followed by closing the mouth, licking the nose and swallowing. The pharyngeal/laryngeal area, as well as the mouth, should be thoroughly assessed for structural abnormalities.

Clinically, it is difficult to distinguish whether regurgitation is a functional disorder or whether a structural abnormality could be responsible. Thorough palpation of the ventral neck area is recommended to assess for any obvious masses. If the neurological examination reveals any further deficits, a functional disorder is more likely.

Assessment of a neuroanatomical cause

Idiopathic cause

If further neurological examination is unremarkable and structural diseases have been excluded, idiopathic megaoesophagus/idiopathic dysphagia must be considered. It is, however, important to bear in mind that megaoesophagus and regurgitation or dysphagia may be the only clinical sign of a more generalized disease. For example, 43% of dogs with MG have only focal manifestations of diseases such as megaoesophagus or dysphagia.

Central/brainstem cause

With brainstem lesions (e.g. tumour or encephalitis), additional neurological deficits, such as altered mentation, postural reaction deficits and multiple CN deficits, are usually present. Spinal reflexes, however, will be normal or increased.

If dysphagia is due to spasms of the pharyngeal muscles, tetanus must be considered; however, further typical signs, such as risus sardonicus (tetanus), rigidity of limbs and trismus, are usually evident.

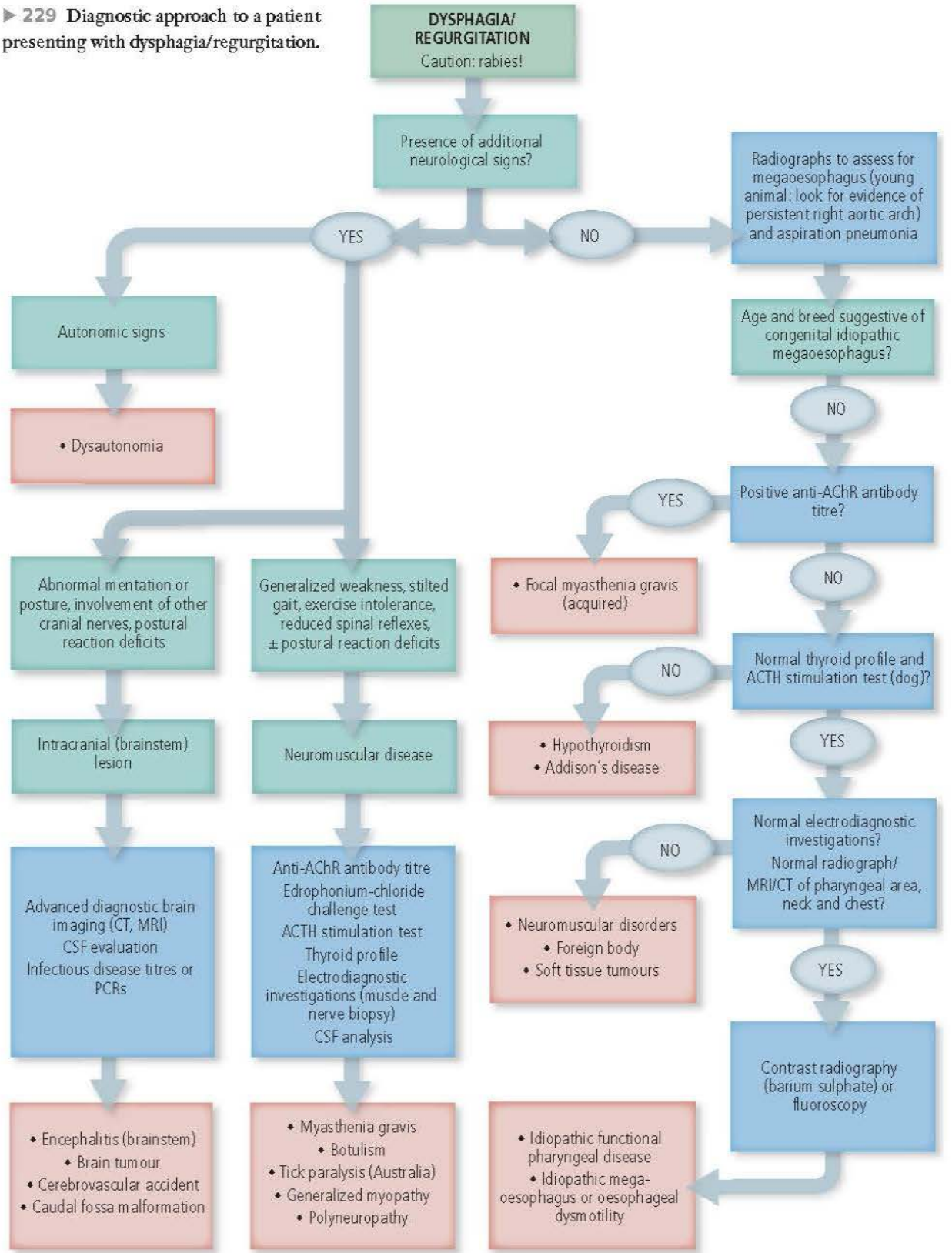
Neuromuscular cause

If generalized LMN signs are present (reduced or absent spinal reflexes), a polyneuropathy or botulism (Chapter 25) must be considered as the underlying cause for dysphagia and/or regurgitation. If generalized weakness and exercise intolerance are present, MG should be high on the list of differential diagnoses. Generalized weakness, together with a stiff gait, often indicates a generalized myopathy. In cases of myotonia, spasms of the pharyngeal muscles can occur; however, further typical signs, including muscle dimpling (percussion myotonia), are usually evident.

Autonomic cause

If regurgitation is due to dysautonomia, additional signs of autonomic dysfunction are likely to be present (see section above).

▶ 229 **Diagnostic approach to a patient presenting with dysphagia/regurgitation.**



Distinguishing prehension disorders from dysphagia

Taking a thorough history will help to distinguish the inability to prehend (trigeminal or hypoglossal nerve dysfunction) from dysphagia (glossopharyngeal and/or vagal nerve dysfunction). If animals have a problem with prehension, they often seemingly spend a lot of time drinking without success; however, owners might report polydipsia. With dysphagia, coughing after drinking and eating will be common and there will be excessive saliva in the pharynx. As the vagus also innervates the larynx, dysphonia and inspiratory stridor might be present in addition to laryngeal paralysis.

Distinguishing regurgitation from vomiting

Regurgitation (vagus nerve dysfunction) must be distinguished from vomiting. This can be achieved with a detailed description by the owners and measurement of the pH of the regurgitated or vomited material (vomit will have an acidic pH and regurgitated material a more basic pH).

Differential diagnosis

The list of differential diagnoses for dysphagia and regurgitation is dependent on the overall clinical and neurological evaluation, as well as on signalment, history and course of the disease. Disease mechanisms and conditions commonly associated with the emergency evaluation of a dog or a cat with dysphagia and regurgitation/megaoesophagus are outlined in *Tables 71* and *72* (pages 296, 297).

Specific diagnostic tests for dysphagia

In any animal with a history of dysphagia, a thorough oral and pharyngeal examination should be performed, if necessary under GA. Extreme care should be taken, as these animals may have rabies. Every animal with regurgitation should have conscious thoracic radiographs to investigate whether megaoesophagus or aspiration pneumonia is visibly present.

If dysphagia/regurgitation is the only presenting sign:

- Thyroid function testing (dog): total T4 and TSH determinations as minimum screening; if inconclusive, also consider free T4, T3 and antithyroid antibodies.
- Electrolyte assessment and ACTH stimulation test to exclude Addison's disease (dog).
- Serum CK to investigate for generalized inflammatory myopathies or muscular dystrophy.
- Anti-AChR antibody titre to exclude acquired MG.
- Electrodiagnostic investigations (EMG, nerve conduction velocity, repetitive nerve stimulation) to exclude generalized myopathies or neuropathies and to assess for junctionopathies.
- Positive contrast radiography (barium sulphate) and fluoroscopy can help determine which part of the swallowing phase is disturbed and demonstrate abnormal oesophageal motility.
- MRI or CT of the pharyngeal area, neck and chest helps to evaluate soft tissue structures and investigate for masses or foreign bodies (especially stick injury).

If there are additional generalized neuromuscular signs (weakness, exercise intolerance, stilted gait, reduced segmental spinal reflexes, reduced postural reactions):

- Thyroid panel (dog; see above).
- ACTH stimulation test to investigate for hypoadrenocorticism.
- Serum CK to investigate for generalized inflammatory myopathies or muscular dystrophy.
- If generalized weakness/exercise intolerance is present, edrophonium chloride challenge test and anti-AChR antibody titres to assess for MG.
- Electrodiagnostic investigations (see above).
- If electrodiagnostic testing is abnormal: thoracic radiographs and abdominal ultrasound to exclude paraneoplastic polyneuropathy or para- or preneoplastic myopathy; CSF analysis and muscle and nerve biopsy.

If additional neurological deficits are present suggesting a structural brain disease:

- Advanced brain imaging (CT or MRI).
- CSF analysis (nucleated cell count and cytology, TP concentration).
- Serum and CSF infectious titres and/or PCR for various infectious organisms, and cultures if indicated.

Table 71 **Causes of dysphagia**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Generalized inflammatory myopathies: immune-mediated polymyositis; infectious aetiology (*Toxoplasma*, *Neospora*, *Borrelia*, rickettsial, hepatozoon), paraneoplastic syndrome Dermatomyositis Sensory ganglioneuritis; protozoal polyradiculoneuritis (*Neospora*) Meningoencephalitis of unknown aetiology (e.g. GME) Infectious encephalitis (rabies, distemper, *Toxoplasma*, *Neospora*, fungal, bacterial, rickettsial) Tonsillitis and pharyngitis (mostly bacterial)	Generalized inflammatory myopathies: immune-mediated polymyositis; infectious aetiology (*Toxoplasma*) Meningoencephalitis of unknown aetiology (presumed immune-mediated; rare) Infectious encephalitis (rabies, FIP, *Toxoplasma*, bacterial, fungal) Tonsillitis and pharyngitis (mostly bacterial)
Trauma	Foreign bodies*	Foreign bodies*
Toxic	Botulism* Tetanus Tick paralysis	Tick paralysis (rare)
Anomalous	Congenital myasthenia gravis Myotonia congenita Hyoid bone abnormality (very rare)	Congenital myasthenia gravis
Metabolic	Hypothyroidism Addison's disease	
Idiopathic	Acquired myasthenia gravis* Cricopharyngeal achalasia	Acquired myasthenia gravis
Neoplastic	Tumours of the neck/throat area Brainstem tumours	Tumours of the neck/throat area Brainstem tumours

* Common cause

Common causes of acute/subacute dysphagia and regurgitation

Idiopathic megaoesophagus

Overview

Idiopathic megaoesophagus occurs as congenital and acquired forms in dogs and is rare in cats. Congenital canine idiopathic megaoesophagus has been reported in Great Danes, German Shepherd Dogs, Irish Setters, Newfoundlands, Shar Peis and Greyhounds and is inherited in Wire-haired Fox Terriers (autosomal recessive) and Miniature Schnauzers (autosomal dominant or 60% penetrance autosomal recessive). In cats there seems to be a predisposition for Siamese and Siamese-related breeds. In many cases of acquired megaoesophagus the cause is unknown and therefore the megaoesophagus is termed idiopathic.

Table 72 **Causes of acute/subacute regurgitation/megaoesophagus**

DISEASE MECHANISM	DOGS	CATS
Inflammatory/infectious	Generalized inflammatory myopathies: (see *Table 71*) Dermatomyositis Sensory ganglioneuritis Meningoencephalitis of unknown aetiology (see *Table 71*) Oesophagitis	Generalized inflammatory myopathies: immune-mediated polymyositis; infectious aetiology (*Toxoplasma*) Meningoencephalitis of unknown aetiology (see *Table 71*; rare) Oesophagitis
Trauma	Foreign bodies*	Foreign bodies*
Toxic	Botulism* Lead or thallium intoxication Tiger snake envenomation Tetanus Acrylamide	Lead or thallium intoxication
Anomalous	Persistent right aortic arch Congenital myasthenia gravis Myotonia congenita (only regurgitation)	Persistent right aortic arch
Metabolic	Addison's disease Hypothyroidism	
Idiopathic	Idiopathic megaoesophagus* Acquired myasthenia gravis* Idiopathic oesophageal dysmotility without megaoesophagus Dysautonomia*	Idiopathic megaoesophagus Acquired myasthenia gravis Idiopathic oesophageal dysmotility without megaoesophagus Dysautonomia*
Neoplastic	Tumours of the neck/chest area Brainstem tumours	Tumours of the neck/chest area Brainstem tumours

* Common cause

Clinical presentation

The most common clinical sign is regurgitation of undigested food. Neurological examination is normal with idiopathic megaoesophagus. The congenital form is usually apparent at the time of weaning and seems to be associated with developmental immaturity of the innervation and/or musculature. For both congenital and acquired idiopathic forms, a selective vagal afferent dysfunction seems to play a major role.

Diagnosis

Underlying neurological/NM disease and structural lesions must be excluded by thorough clinical and neurological evaluation and further diagnostic work-up before making a diagnosis of idiopathic megaoesophagus.

Diagnosis is based on the history of regurgitation and radiographic evidence of oesophageal dilation. A normal oesophageal motility can be demonstrated by contrast radiography and fluoroscopy. Concurrent aspiration pneumonia must be excluded radiographically.

Management

The management of animals with idiopathic megaoesophagus includes feeding and drinking from a height and/or with a gastrostomy tube. Appropriate nutrition and hydration need to be assured at all times. Aspiration pneumonia needs to be addressed if present. Certain medical therapies have been advocated for stimulating oesophageal peristalsis (e.g. metoclopramide or cisapride) or diminishing lower oesophageal sphincter tone (e.g. anti-cholinergics or calcium channel antagonists); however, the results have been rather disappointing. Metoclopramide and cisapride are smooth muscle prokinetic agents and therefore not likely to have much of an effect on the oesophagus, especially in dogs, and risk too many side-effects (e.g. calcium channel antagonists have potent hypotensive effects).

The prognosis for congenital idiopathic megaoesophagus is usually guarded. Acquired idiopathic megaoesophagus generally has a poor prognosis for recovery, although spontaneous recovery has been reported sporadically.

Rabies

Overview

Rabies, a notifiable disease in certain countries, is the most important zoonotic infection and is caused by a rhabdovirus (genus Lyssavirus). (See also Chapter 19.) It is characterized by a non-suppurative polioencephalomyelitis and craniospinal neuritis. All warm-blooded species are susceptible to rabies. Rabies occurs in many countries, even though transmission through dogs and cats plays a much lower role in developed countries due to vaccination regimes. Transmission occurs through bite wounds (rarely other wounds), via the saliva of infected animals. After local replication in the muscle, the highly neurotrophic virus travels to the CNS via the peripheral nerves. Once the CNS is infected, the virus spreads centrifugally via peripheral nerves to other organs (including the salivary glands). Incubation time may be anything from 2–3 weeks to up to 6 months, depending on the site of inoculation, the amount of virus transmitted, the viral strain and the animal's immune status.

Clinical presentation

Initial clinical signs in dogs and cats may be non-specific and include temperament change and excessive salivation. After 2–5 days, signs will progress to either the furious form (aggression, restlessness, howling, salivation, sometimes convulsions) or the dumb-paralytic form characterized by progressive ascending paresis/paralysis, dropped jaw, pharyngeal and hypoglossal paralysis with subsequent dysphagia and drooling of saliva, and facial paralysis. Regurgitation is not a typical sign, but can occur as well if the brainstem is affected.

Diagnosis

Diagnosis is confirmed post mortem. Most animals will reveal typical inclusions (Negri bodies); however, definitive diagnosis depends on positive results of additional tests such as immunohistochemistry and PCR.

Management

There is no treatment for rabies. Animals exposed to rabies that have not been vaccinated must be euthanized. If animals are currently vaccinated and have been exposed, they should be re-vaccinated and closely confined under observation for at least 3 months. If humans are exposed to rabies and they are unvaccinated, post-exposure prophylaxis with immunoglobulins must be implemented.

Myasthenia gravis

See Chapter 24.

Dysautonomia

See Anisocoria, above.

Botulism

See Chapter 25.

Generalized inflammatory myopathies

See Chapter 8.

MONOPARESIS AND NEUROLOGICAL CAUSES OF LAMENESS

Toby Gemmill & Malcolm McKee

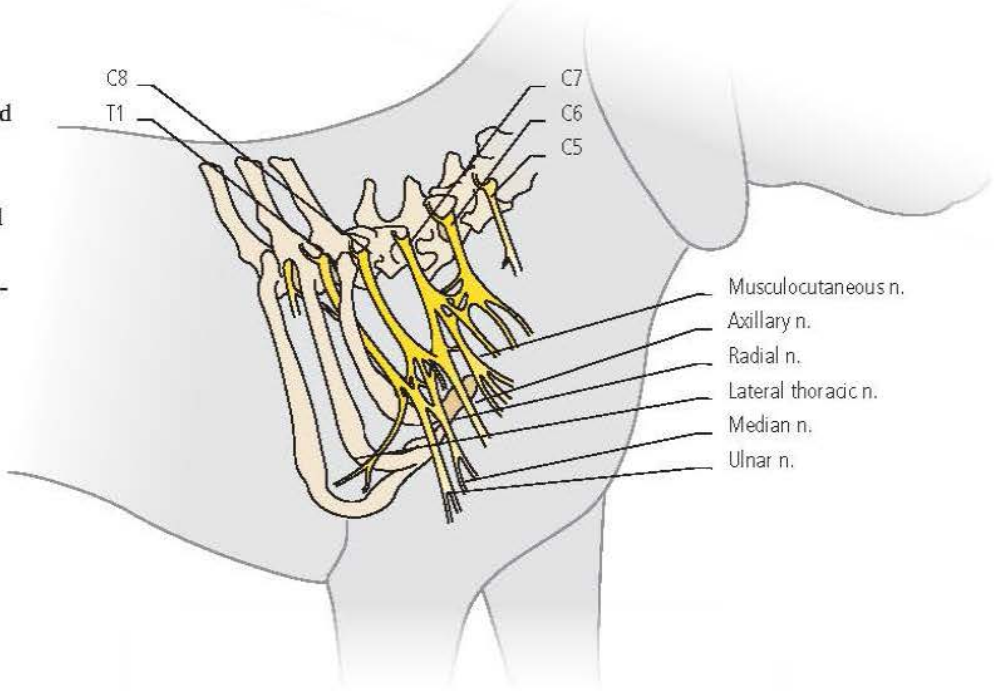
INTRODUCTION

Animals with dysfunction of a limb can be broadly divided into cases exhibiting lameness and those suffering paresis and/or ataxia. In general, most causes of lameness are orthopaedic in origin, whereas most causes of paresis are neurological. However, these distinctions are not clear-cut and diagnosing the cause of limb dysfunction can be challenging in some cases. For example, apparent paresis can on occasion be due to orthopaedic conditions such as hip dysplasia or an avulsion fracture. In contrast, lameness in some patients can be attributed to neurological conditions such as radiculopathies or peripheral nerve lesions. Furthermore, it is not uncommon to encounter cases with concurrent orthopaedic and neurological conditions (e.g. animals with fractures and concurrent peripheral nerve injuries). It is vital in such cases to make an accurate diagnosis and to establish the relative importance of different lesions as they relate to management options and prognosis.

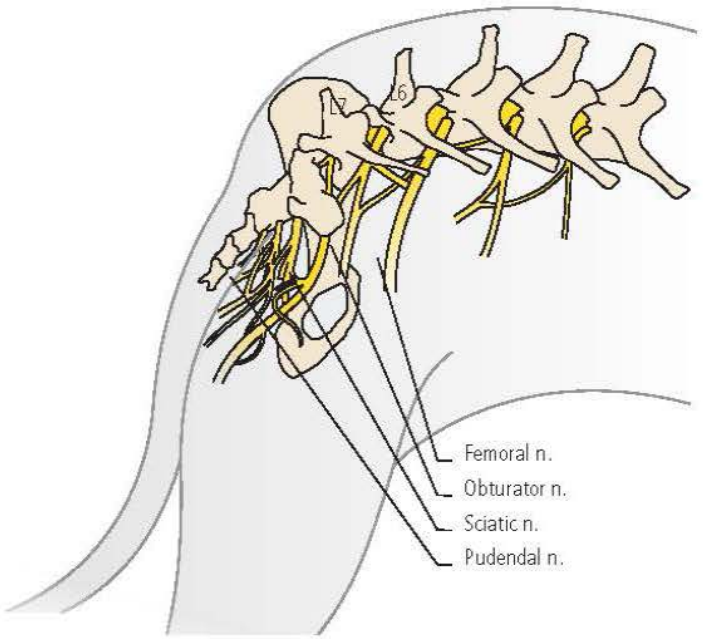
NEUROANATOMICAL BASIS

The UMN system is confined to the CNS. It is responsible for the initiation and maintenance of normal movements and for the maintenance of tone in extensor muscles to support the body. UMN cell bodies lie within the cerebral cortex, basal nuclei, brainstem or spinal cord. Axons travel through the brain and/or spinal cord white matter and synapse indirectly via an interneuron with an LMN to modulate its activity.

The LMN system connects the CNS with the muscle to be innervated. Its cell bodies lie mainly within the ventral horn of the spinal cord grey matter in the cervical and lumbar intumescences (spinal cord segments C6–T2 and L4–S3, respectively). Axons exit the spinal cord via the ventral nerve roots and coalesce with sensory dorsal nerve roots to form a spinal nerve. These spinal nerves then course into the brachial or lumbosacral plexus, where they form peripheral nerves, which then innervate specific regions of the limbs (**230; 231,** next page).



▶ **230** **Spinal and peripheral nerves associated with the brachial plexus: lateral thoracic; ulnar; median; radial; axillary; and musculocutaneous nerves. The subscapular and suprascapular nerves arise immediately cranial to the musculocutaneous nerves.**



▲ **231** Spinal and peripheral nerves associated with the lumbosacral plexus: femoral; obturator; sciatic; and pudendal nerves.



▲ **232** Ventrodorsal view of a cervical myelogram. Compression of the spinal cord over the C2/C3 disc space compatible with disc extrusion can be seen (arrow). The dog was presented with left forelimb paresis. On clinical examination very subtle left hindlimb proprioceptive deficits were also apparent.

Spinal cord lesions are less likely to produce true monoparesis and/or lameness as opposed to lesions affecting the nerve roots, spinal nerves, plexi and peripheral nerves. Lesions affecting spinal cord segments C1–C5 (**232**) tend to cause UMN paresis and GP ataxia, which can occasionally appear to affect the function of just one forelimb. Lesions affecting C6–T2 segments may cause LMN paresis in a forelimb, although frequently UMN paresis and GP ataxia can be appreciated affecting the ipsilateral hindlimb. Lesions located at T3–L3 segments may cause UMN paresis and GP ataxia in one or both hindlimbs. Lesions affecting L4–S1 segments may cause LMN paresis affecting one or both hindlimbs.

Sensory deficits are also observed in most cases involving the LMN, and these may help in mapping out the area of denervation. The clinical signs of LMN dysfunction include rapid and pronounced muscle atrophy, hypotonia, hyporeflexia, paresis and/or lameness (see Chapter 10). It is often possible to localize a lesion to a specific peripheral nerve based on loss of specific spinal reflexes, involvement of specific muscle groups and/or cutaneous sensory testing of specific regions of the limbs. Knowledge of the motor and sensory functions of different peripheral nerves is therefore essential in lesion localization.

Forelimb innervation

The brachial plexus is derived from spinal cord segments C6–T1, with minor contributions from C5 and T2 (see **230**). The important nerves of the plexus, from cranial to caudal, include the suprascapular, musculocutaneous, axillary, radial, median and ulnar nerves (*Table 73*). The median and ulnar nerves exit the plexus as

Table 73 **Limb innervation**

NERVE	SPINAL CORD SEGMENTS	MUSCLES INNERVATED	CUTANEOUS SENSORY FIELD	SEGMENTAL SPINAL REFLEX
THORACIC LIMB				
Suprascapular	C6, 7	Supra- and infraspinatus	Lateral aspect of shoulder	None
Subscapular	C6, 7	Subscapularis	None	None
Musculocutaneous	C6, 7, 8	Biceps brachii, brachialis, coracobrachialis	Medial aspect of proximal antebrachium and first digit	Biceps reflex, withdrawal reflex (flexion of elbow)
Axillary	C7, 8	Deltoid, teres major and minor	None	None
Radial	(C6) C7, 8, T1, (2)	Triceps brachii, extensors of carpus and digits	Cranial aspect of antebrachium, dorsal aspect of paw	Triceps reflex (proximal) and extensor carpi radialis (distal)
Median and ulnar	C8, T1, (2)	Flexors of carpus and digits	Caudal aspect of antebrachium, palmar aspect of paw, lateral aspect of 5th digit	Withdrawal reflex (flexion of carpus and digits)
HINDLIMB				
Femoral	L4, 5, 6	Quadriceps group Psoas group	Medial aspect of thigh and crus, first digit	Patellar reflex
Obturator	(L4), 5, 6	Adductors	None	None
Sciatic nerve	L6, 7, S1, (2)	Biceps femoris, gastrocnemius, cranial tibial, semitendinosus, semimembranosus	Entire limb (via tibial and peroneal branch) except for medial aspect and first digit	Withdrawal reflex (stifle flexion)
Tibial nerve	L6–S1	Tarsal extensors, digital flexors	Plantar aspect of metatarsus and paw	Gastrocnemius reflex
Peroneal nerve	L7–S1	Tarsal flexors, digital extensors	Dorsal aspect of metatarsus and paw	Cranial tibial reflex, withdrawal reflex (hock flexion)
Pelvic nerve	S1–S3	Parasympathetic supply to pelvic viscera	None	None
Pudendal nerve	S1–S3	External anal sphincter	Perineum, external genitalia	Perineal reflex

a single bundle, but separate into two distinct nerves at the level of the mid-humerus. The lateral thoracic nerve, originating from spinal cord segments C8–T1, supplies motor innervation to the cutaneous trunci muscle. Pre-ganglionic sympathetic fibres supplying innervation to the eye originate from the T1–T3 spinal cord segments. These pre-ganglionic neurons destined for the head leave the spinal cord in the segmental ramus communicans, which joins the thoracic sympathetic trunk (see Chapter 15).

Hindlimb innervation

The lumbosacral plexus is derived from the L4–S2 spinal cord segments, with a small contribution from the S3 segment (see **231**). Because of the foreshortening of the spinal cord with respect to the lumbar spine, these spinal cord segments lie between the L3 and L5 vertebral bodies. In cats and smaller dogs the spinal cord can terminate slightly further caudally, with the S3 segments lying adjacent to the cranial border of the vertebral body of L6. Peripheral nerves arising from the lumbosacral plexus include the femoral, obturator, sciatic, pelvic and pudendal nerves (*Table 73*). The sciatic nerve divides at the level of the distal femur into the peroneal and tibial nerves.

Table 74 **Neurological causes of monoparesis and lameness**

DISEASE MECHANISM	DOGS AND CATS
Vascular	Ischaemic myelopathy Ischaemic neuromyopathy (aortic or brachial artery thromboembolism)
Inflammatory/infectious	Hypertrophic neuritis Plexus neuritis Discospondylitis Myelitis/meningomyelitis Neosporosis radiculitis/myositis
Trauma	Plexus avulsion Peripheral nerve trauma
Toxic	Localized tetanus
Neoplastic	Peripheral nerve sheath tumour Local invasion of nerves by adjacent tumours Lymphoma
Degenerative	Lateralized intervertebral disc extrusion or protrusion Foraminal stenosis

Table 75 **Acute and subacute orthopaedic causes of lameness**

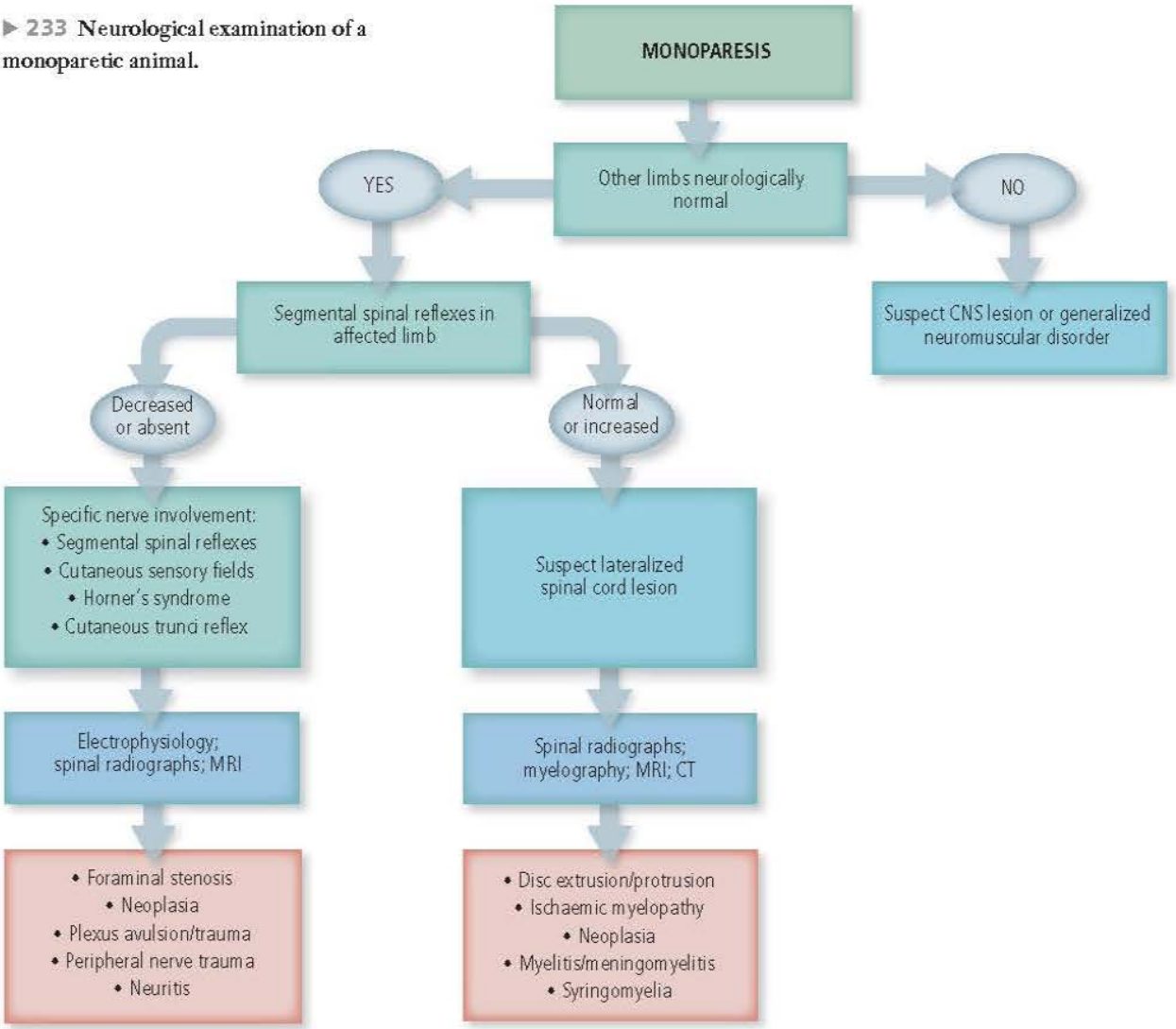
DISEASE MECHANISM	DIFFERENTIAL DIAGNOSES
Inflammatory/infectious	Osteomyelitis Septic arthritis Immune-mediated arthritis
Trauma	Fractures, luxation, joint instability, soft tissue sprains and strains
Toxic	Snake bite
Anomalous	Incomplete ossification of the humeral condyle or radial carpal bones
Metabolic	Pathological fracture secondary to metabolic bone disease
Idiopathic	Panosteitis, metaphyseal osteopathy, Legg–Perthes disease, fibrotic myopathy
Neoplastic	Primary or secondary neoplasia of bone or soft tissues
Nutritional	Pathological fracture secondary to nutritional hyperparathyroidism
Degenerative	Hip dysplasia, cranial cruciate ligament deficiency, patellar luxation, degenerative tendinopathy

DIFFERENTIAL DIAGNOSIS

The differential diagnoses depend implicitly on the anatomical localization of the problem. However, specific neurological deficits may not be apparent in some cases presented for lameness. Furthermore, these patients can sometimes be in significant discomfort, making accurate localization of a source of pain challenging. Differential diagnoses for acute monoparesis or neurological causes of lameness are detailed below and outlined in *Table 74*. Common orthopaedic causes of acute-onset lameness are listed in *Table 75*.

ORTHOPAEDIC AND NEUROLOGICAL EXAMINATION

A detailed history and thorough clinical examination are essential (**233; 234,** *next page*). The signalment of an animal can be suggestive of particular problems; for example, forelimb lameness in a young Rottweiler might raise an index of suspicion for elbow dysplasia. On the other hand, rapid-onset lameness in a middle-aged Cocker Spaniel could be suggestive of IVDD causing a foraminal compression. Features that can be associated with neurological conditions include a history of



▶ **233 Neurological examination of a monoparetic animal.**

▶ **234** **Examination of an animal with a single limb lameness.**

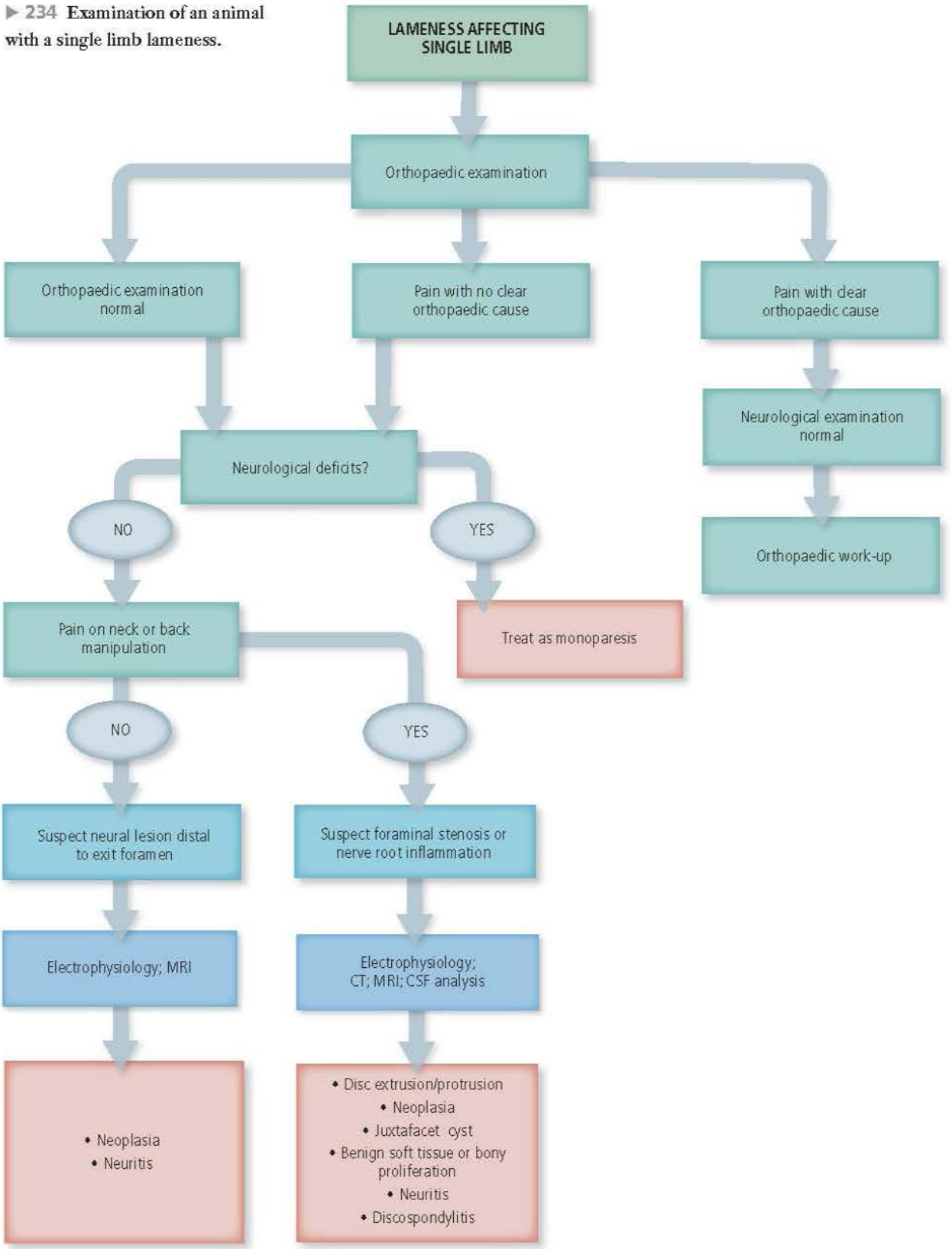


Table 76 Clinical signs suggestive of neurological causes of lameness

- Unprovoked vocalization
- Arching of the back
- Low head carriage
- Reluctance to lower head to eat from the floor
- Reluctance to allow manipulation of the neck
- Pain on palpation of the spine

stumbling or ataxia, low head carriage, an arched back and holding an affected limb high off the ground rather than exhibiting a weight-bearing lameness (*Table 76*). It is important to question owners carefully to ensure these features are not overlooked.

Following a general clinical examination, detailed orthopaedic and neurological examinations should then be performed. In most cases this will allow the clinician to establish whether a problem is orthopaedic or neurological in nature and to establish the anatomical origin of the problem. If a neurological lesion is suspected, it is important to identify whether it is UMN or LMN in nature, and whether it is originating from the brain, the spinal cord, the nerve roots or a peripheral nerve.

Initial assessment of the gait allows the clinician to determine which limb or limbs is/are affected and to gain an impression of the severity of the problem. It is possible in most cases to establish from observing the gait whether the principal problem is lameness, which often suggests an orthopaedic problem, or weakness, which is more suggestive of neurological disease.

Shortened stride length is frequently associated with decreased muscle tone or pain, which would be more commonly associated with LMN lesions or orthopaedic disease, respectively. In contrast, UMN lesions can be associated with increased stride length or hypermetria. Compared with UMN paresis, disorders of the LMN often only result in paresis and not in ataxia. Although most peripheral neuropathies affect both motor and sensory axons, the gait dysfunction principally reflects LMN paresis. The degree of paresis varies from a short stride to complete inability to support weight, causing collapse of the limb whenever weight is placed on it.

Orthopaedic examination

Following gait analysis, each limb should be systematically examined. Limbs should be palpated to assess muscle mass and symmetry. LMN lesions often lead to dramatic muscle atrophy (**235**); this can be very specific depending on the peripheral nerves involved. Each limb should then be evaluated, working distally to proximally. Each joint, ligament, tendon and bone should be carefully assessed for evidence of pain, restricted range of motion, instability and swelling. To help localize a source of pain it can be helpful in excitable patients to repeat this examination following administration of a mild sedative (e.g. using a combination of acepromazine/butorphanol). An animal exhibiting lameness, but with a normal orthopaedic examination, should immediately raise an index of suspicion for a possible neurological lesion. For the forelimb, deep palpation of the axilla may help localize discomfort to the brachial plexus. Discomfort on traction of the limb (pulling the limb distally) can be suggestive of a lesion affecting neural structures of the proximal limb. Arterial pulses should be palpated proximally and distally to exclude vascular lesions. Finally, a rectal examination can be performed, which may allow palpation of a mass affecting the lumbosacral trunk.



▲ **235** Severe supra- and infraspinatus muscle atrophy in a dog, secondary to a peripheral nerve sheath tumour (cranial to left of picture, caudal to right).

Neurological examination

The neurological examination consists of assessment of gait, posture, mentation, CN function, postural reactions and segmental spinal reflexes. Cutaneous sensation of different peripheral nerves of the dysfunctional limb should be tested, although this is accepted to be a subjective behavioural assessment in many dogs (see Chapter 10). The eyes should be assessed for evidence of Horner's syndrome, which can be caused by a lesion affecting the caudal part of the brachial plexus (T1–T3 nerve roots). The C8 and T1 nerve roots supplying the lateral thoracic nerve can also be affected in these cases, leading to ipsilateral loss of the cutaneous trunci (panniculus) reflex.

Any paresis should be characterized as UMN or LMN in origin where possible. Most neurological lesions causing monoparesis or lameness affect spinal nerve roots or peripheral nerves rather than the CNS. Therefore, any deficits tend to be LMN in nature. It should be borne in mind that lateralized spinal cord lesions (**236**) can also produce monoparesis, although in most cases involvement of more than one limb can be appreciated.

For the forelimbs, the triceps and extensor carpi radialis reflexes are helpful for assessing the radial nerve proximally and distally, respectively. These reflexes are often considered subjective tests, especially in small dogs. Weakness in elbow flexion, suggesting a musculocutaneous deficit, and weakness in carpal flexion, suggesting median nerve dysfunction, can be assessed using the withdrawal reflex.

For the hindlimbs, the femoral nerve can be assessed using the patellar reflex or extensor tone of the quadriceps. The sensory zone innervated by this nerve is the medial aspect of the proximal limb. The cranial tibial reflex is useful in assessing the peroneal nerve; the tibial nerve can be tested using the gastrocnemius tendon reflex. The withdrawal reflex is useful in assessing the sensory function of different nerves as well as sciatic motor function. This can be accompanied by a neurogenic atrophy and an altered stance (**237**). Obturator nerve dysfunction leads to a failure to maintain adduction of the limb on slippery surfaces, although this can be difficult to appreciate, as dogs and cats can adapt their gait surprisingly well to accommodate for obturator deficits. Although not a cause of paresis or lameness, pudendal nerve dysfunction can be tested with the anal reflex and by assessment of perineal sensation.



▲ **236** Ventrodorsal view of a thoracolumbar myelogram of a dog presented with right hindlimb paresis. An extradural compressive lesion caused by neoplasia is identified at the level of L4 (arrow).



▲ **237** Sciatic nerve dysfunction causing plantigrade stance and loss of muscle mass in the proximal limb.

DIAGNOSTIC TESTS

Once the anatomical source of a particular problem has been established, further investigations can be considered. It is important that any abnormalities are interpreted in the light of the original history and clinical examination; it is common to identify multiple abnormalities on diagnostic tests, many of which may not be clinically significant.

Plain radiographs

- Orthogonal radiographs are useful to assess vertebral structures and disc spaces.
- Oblique projections of the spine can be useful to identify foraminal disc extrusions. This is especially true for the cervical spine if extruded material is mineralized.
- Occasionally, neoplastic lesions can cause enlargement of the intervertebral foramen due to pressure atrophy of the bone.
- Thoracic radiographs are useful as part of tumour staging.

Myelography

- Useful to assess spinal cord morphology, but is frequently unhelpful for identifying foraminal stenosis or nerve root or peripheral nerve lesions (**236**).

Computed tomography

- Can be helpful to assess the spinal cord or identify mineralized disc extrusions.
- Especially useful for assessing spinal cord compression when combined with myelography. Transverse views help to evaluate foraminal stenosis.
- Resolution is generally not good enough to assess peripheral nerves unless they are enlarged due to neoplasia or are associated with osseous lysis.

Magnetic resonance imaging

- Imaging modality of choice for spinal cord, nerve root, plexus and peripheral nerve lesions.

Ultrasonography

- May allow identification of brachial plexus tumours and subsequent investigation with fine-needle aspiration.

Electrophysiological studies

- EMG is helpful in some cases to support neurological involvement, particularly in cases of occult lameness where an orthopaedic cause cannot be identified.
- Spontaneous electrical activity often develops in denervated muscles 7–10 days after the nerve injury has occurred.
- EMG alone does not differentiate primary muscular disease from peripheral nerve disease.
- Nerve conduction studies can be used to assess specific spinal nerves. F-waves and cord dorsum potentials can give information on ventral and dorsal nerve roots, respectively.

CSF analysis

- Useful to exclude inflammatory CNS disease.
- Collection distal to the site of the suspected lesion is more likely to reveal any significant changes.
- Nerve root compression may result in increased CSF protein levels.
- CSF PCR and evaluation of antibody titres can be useful to assess for specific conditions such as neosporosis or toxoplasmosis.

Histopathology

- Can be used to make a definitive diagnosis of a lesion.
- Biopsies should be guided by the results of previous imaging studies.
- Biopsy of neural tissue must be considered carefully with respect to the potential iatrogenic morbidity.

Synovial fluid analysis

- Useful to exclude inflammatory arthritis.
- Can also help support a diagnosis of osteoarthritis, although results should be interpreted with caution since this is frequently an incidental condition.

COMMON ACUTE/SUBACUTE CAUSES OF FORELIMB MONOPARESIS

Brachial plexus avulsion

Overview

Brachial plexus avulsion is the most common traumatic peripheral neuropathy in the dog. It results from forced abduction of the forelimb and subsequent stretching or tearing of nerve roots, often following a road traffic accident or a fall. The condition may affect the cranial (C6/7) or caudal (C8/T1) nerve roots in isolation or can involve the entire brachial plexus. It is more commonly unilateral than bilateral. Three types of lesion can be distinguished depending on the degree of nerve damage:

- Neurapraxia is a transient, physiological failure of nerve transmission in the absence of structural damage.
- Axonotmesis is disruption of the axons, with the endoneurial and Schwann cell myelin sheaths remaining intact.
- Neurotmesis is complete severance of all structures of the nerve (axons, Schwann cells and supporting connective tissue).

Damage most often occurs at the level of the spinal nerve roots where resistance to stretch is less than in peripheral nerves owing to the lack of perineurium.

Clinical presentation

Clinical signs vary depending on which peripheral nerves are involved and the severity of the injury. They relate to LMN paresis with or without associated cutaneous sensory loss. Avulsion of the cranial plexus roots (C6/C7 nerve roots) results in a loss of shoulder movement and elbow flexion, although the animal can still bear weight on the limb as elbow extension is spared. Cutaneous sensation may be lost over the craniomedial aspect of the antebrachium.

Avulsion of the caudal plexus roots (C8–T2 nerve roots) results in carriage of the limb with the elbow and shoulder flexed. The animal cannot bear weight because of triceps brachii muscle paralysis. The elbow is dropped and the carpus knuckled (**238**). Cutaneous sensation may be lost distal to the elbow and over the caudolateral aspect of the antebrachium.



▲ **238** **Carpal flexion in a dog secondary to a caudal brachial plexus avulsion.**

Complete avulsion of all plexus roots (C6–T2 nerve roots) causes a flaccid limb with an inability to bear weight and loss of cutaneous sensation in the entire limb. Ipsilateral Horner's syndrome and/or loss of the cutaneous trunci reflex is often seen if the caudal brachial plexus is affected.

Diagnosis

Diagnosis can be primarily based on historical and clinical findings. EMG helps to document the extent of muscle denervation and confirms the distribution of nerve injury, although changes may not be seen for 7–10 days after the injury. CT evaluation would assist in ruling out associated traumatic vertebral lesions. MRI may help rule out other causes if a traumatic aetiology cannot be confirmed, and it can identify nerve root abnormalities secondary to trauma.

Management

Treatment is usually conservative and relies mainly on aggressive physiotherapy. Patients should be monitored for complications such as self-mutilation, excoriation of the digits, trophic ulcers and muscle contractures. Gabapentin (10–20 mg/kg PO q8–12h) can be considered to control neuropathic pain if self-mutilation is seen.

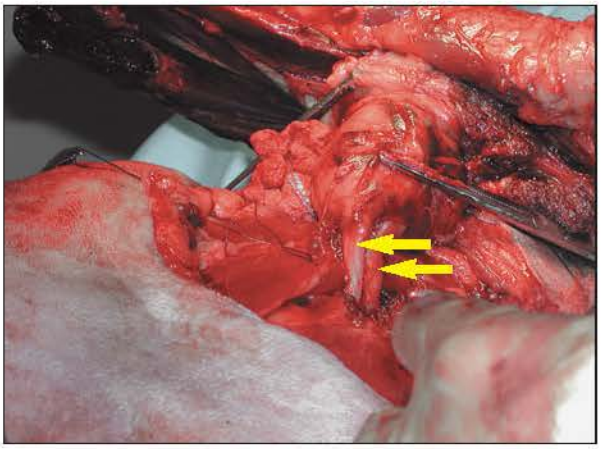
Tendon transposition procedures can be considered to restore elbow or carpal function. Careful case selection is essential and any muscle to be transposed should have its function assessed using electrophysiology prior to surgery. Pancarpal arthrodesis, to prevent carpal collapse secondary to loss of radial nerve function, is rarely appropriate since in most cases elbow function is also absent. Amputation should be considered in more severely affected cases or if complications develop. As this is a 'salvage' procedure, it is prudent in most cases to wait 2–3 months after the injury before such a decision is made.

The prognosis depends on the extent of the avulsion. Nerve transection has a poor prognosis, whereas dogs suffering neurapraxia can recover. Clinically poor prognostic indicators include evidence of a caudal or complete avulsion, loss of nociception and no evidence of a return of function within 1–2 months. The outcome is often acceptable for animals with cranial avulsions that are able to bear weight and maintain sensation over the distal part of the limb. Serial evaluation of radial motor nerve conduction velocity may be a useful prognostic indicator. Early decreased conduction velocity is associated with a poor outcome.

Peripheral nerve sheath tumours

Overview

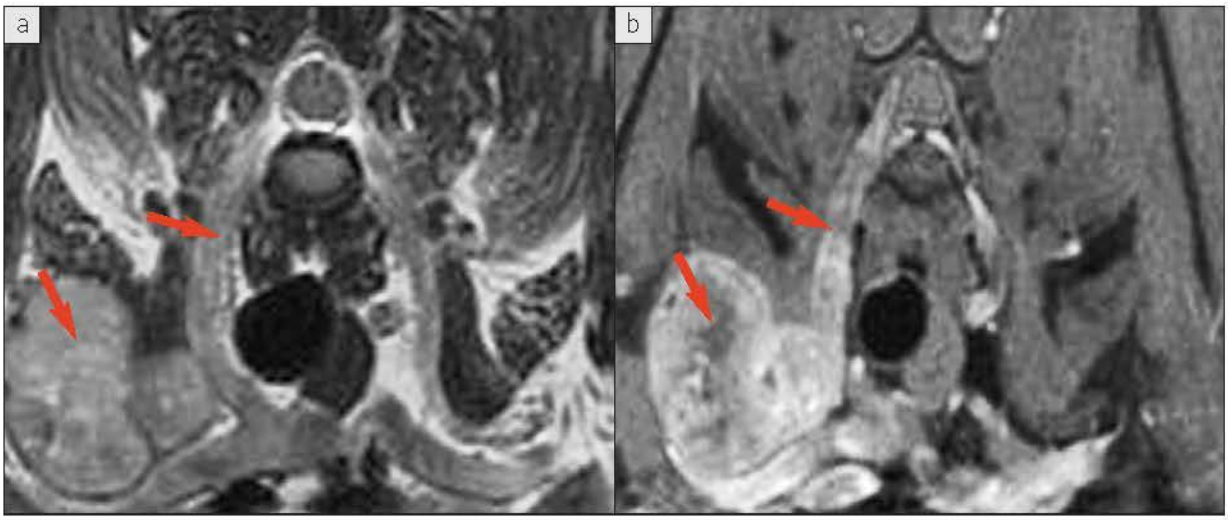
Peripheral nerve sheath tumours arise from cells surrounding the axons in peripheral nerves or nerve roots and are frequently malignant. Tumours spread proximally towards the spinal cord (**239**). They usually present with severe, progressive lameness, marked muscle atrophy and pain. They rarely present with acute monoparesis (**240**). Neurological deficits are seen late in the clinical course, if at all. Deep palpation of the axilla can allow identification of a mass in some cases. Electrophysiological studies, and in particular EMG, can be supportive of neural involvement, but may be unremarkable early in the disease.



▲ **239** Intraoperative image of a forelimb amputation demonstrating grossly thickened spinal nerves secondary to proximal extension of a peripheral nerve sheath tumour (arrows).



▲ **240** Right forelimb proprioceptive deficits in a dog with a peripheral nerve sheath tumour.



▲ **241** **MR images showing a peripheral nerve sheath tumour (arrows): T2-weighted (a); post contrast T1-weighted (b).**

Diagnosis

Diagnosis is usually confirmed with MRI (**241**). Ultrasound can help to identify more peripherally located lesions (e.g. axilla) and may allow fine-needle aspiration of the lesion.

Management

Local excision is usually unrewarding due to postoperative brachial plexus dysfunction and tumour recurrence. Forelimb amputation with proximal excision of nerve roots is the treatment of choice in many cases. This can be combined with a hemilaminectomy, durotomy and rhizotomy if there is evidence of spinal nerve and/or nerve root involvement.

The prognosis is guarded as invasion of the spinal cord often occurs prior to diagnosis. Recurrences are common following resection of peripherally located tumours and in one report the average time to recurrence was 5 months.

Radial nerve injury

Overview

Proximal injury to the radial nerve is usually associated with fractures of the first rib and leads to loss of elbow, carpal and digital extension. Distal injury is often caused by humeral fractures.

Clinical presentation

The elbow is 'dropped' and the animal walks with the carpus and digits knuckled over. Elbow function may be preserved with injury located distal to the branches that supply the triceps muscle. Clinical signs in these cases include knuckling of the paw, carpal collapse and loss of cutaneous sensation in the cranial aspect of the limb distal to the injury.

Diagnosis

Diagnosis is usually made on clinical grounds.

Management

Appropriate treatment of any orthopaedic injuries should be carried out. Treatment of the neurological injury is conservative in most cases and based on aggressive physiotherapy to preserve joint motion and delay muscle atrophy. If nerve dysfunction is persistent, and triceps function is retained, tendon transposition procedures or carpal arthrodesis can be considered.

The prognosis for distal lesions depends on the severity of the neural injury. Neurapraxia is more common and most cases recover within 1–2 months. Neurotmesis leads to complete loss of cutaneous sensation over the cranial antebrachium and foot and carries a poor prognosis.

Foraminal stenosis

Overview

Pressure on neural structures within intervertebral foramina can lead to lameness or paresis. Causes of foraminal stenosis include:

- Lateralized disc extrusion or protrusion.
- Juxtafacet cysts.
- Joint capsule hypertrophy of articular facets.
- Benign new bone formation around the margins of the foramen.
- Discospondylitis.
- Any neoplasm causing relative stenosis of the intervertebral foramen.

Clinical presentation

Animals may be presented with acute or chronic history. Clinical features may include: pain on manipulation of the neck; LMN paresis localizing to one or more nerves; sensory signs such as conscious proprioceptive deficits and areas of cutaneous hypoaesthesia or analgesia; and/or 'nerve root signature' manifested as pain on manipulation of the limb, lameness or non-weight bearing on the affected limb.

Diagnosis

Diagnosis often requires advanced imaging modalities to assess the intervertebral foramina and epidural spaces. EMG may reveal spontaneous electrical activity in the muscles innervated by the affected nerve; however, this is non-specific.

Management

Conservative treatment is successful in mild cases. This consists mostly of strict rest for 4 weeks and anti-inflammatory drugs (steroidal or non-steroidal) to help alleviate signs of radicular pain. Other pain management modalities include acupuncture, gabapentin (10–20 mg/kg PO q8–12h) and muscle relaxants such as methocarbamol (20–45 mg/kg PO q8–12h).

Surgery may be required for more severe cases or those refractory to conservative management. Direct decompression (via dorsal laminectomy plus facetectomy or foraminotomy) or indirect decompression via vertebral distraction–fusion can be considered.

Many cases respond well to conservative therapy. Neoplasia carries a poor prognosis.

Brachial plexus neuritis

Overview

Brachial plexus neuritis is a rare, usually bilateral, symmetrical condition. It is thought to be immune mediated and has been occasionally associated with modified live rabies vaccination, *Mycobacterium* infection in cats or eating horse meat. The condition may be part of a more diffuse polyneuropathy.

Clinical presentation

Clinical signs are usually very acute and LMN in nature, leading to flaccid paralysis. A less severe form has been reported with clinical features including a shifting forelimb lameness.

Diagnosis

A presumptive diagnosis is based on MRI findings. Brachial plexus neuritis can be difficult to distinguish from neoplasia and therefore histopathology is necessary for a definitive diagnosis. CSF changes may be seen in some cases (elevated protein and pleocytosis). Electrophysiology can confirm axonal dysfunction.

Management

Milder cases may respond to corticosteroid treatment at decreasing doses. The prognosis is poor.

Lymphoma

Overview

Lymphoma has been reported to affect the brachial plexus and is most commonly seen in cats (**242**). It can be unilateral or bilateral and is usually chronic in onset.

Diagnosis

Diagnosis is based on MRI and fine-needle aspirate cytology ± CSF analysis (**243**).

Management

The prognosis is poor, as most cases fail to respond to chemotherapy.



▲ **242** Right forelimb proprioceptive deficits in a cat with lymphoma affecting the brachial plexus.

▶ **243** Cerebrospinal fluid cytology demonstrating a homogeneous lymphocytic pleocytosis characteristic of lymphoma.

Spinal cord lesions

Overview

Rarely, spinal cord conditions can appear predominantly to affect one forelimb. Spinal cord lesions usually cause paresis. Lameness is usually due to concurrent foraminal nerve compression. Neurological examination will often reveal clinical signs involving more than one limb, although these signs can be subtle. Differential diagnoses include disc extrusion or protrusion (compressive), traumatic (minimally compressive) disc herniation, ischaemic myelopathy, syringomyelia, inflammatory CNS disease and spinal cord neoplasia.

COMMON ACUTE/SUBACUTE CAUSES OF HINDLIMB MONOPARESIS

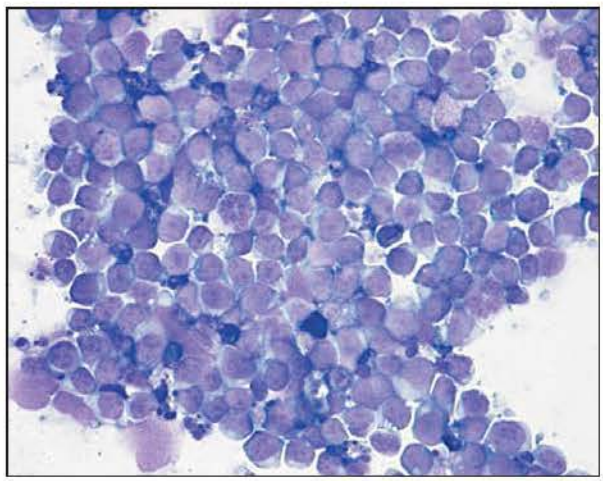
Spinal cord and cauda equina lesions

Overview

As with the cervical spine, thoracolumbar spinal cord lesions can appear to affect predominantly one limb. This is more common with vascular disorders such as ischaemic myelopathy.

Clinical presentation

Clinical signs include paresis or lameness associated with individual nerves. Cauda equina lesions may affect other regional nerves, leading to associated signs such as tail paresis, loss of perineal sensation and urinary and/or faecal incontinence. Lesions at T3–L3 tend to produce





▲ **244** **Right pelvic nerve root signature in a dog with degenerative lumbosacral stenosis. Foraminal compression of the L7 spinal nerve was identified using MRI and confirmed at surgery.**

UMN paresis and GP ataxia; those at L4–S2 produce LMN paresis. Differential diagnoses are similar to those of cervical spinal lesions. In addition, lumbosacral discospondylitis can cause paresis/lameness of one hindlimb.

Foraminal stenosis

Overview

Foraminal compression of nerves forming the lumbosacral plexus (essentially femoral and sciatic nerve contributors) can cause paresis or lameness.

Clinical presentation

Clinical signs relate to the specific nerve roots or spinal nerves involved. Lesions affecting L4–L6 tend to cause femoral nerve deficits; those at L7–S2 tend to cause sciatic deficits. The L7/S1 intervertebral foramen is the most commonly affected site, often associated with degenerative lumbosacral stenosis (**244**). Differential diagnoses are the same as for cervical foraminal stenosis.

Management

Conservative treatment is reserved for mild cases and consists of the same modalities as described for cervical foraminal stenosis. Surgical decompression via hemilaminectomy (+/- facetectomy or foraminotomy) may be necessary for more severe cases. Treatment by lumbosacral fusion or distraction–fusion has also been suggested in dynamic lesions of these lumbosacral vertebrae.

Sciatic nerve injury

Overview

Sciatic nerve injury can be associated with trauma (femoral or pelvic fracture), impingement from a femoral intramedullary pin, entrapment by a suture following perineal herniorrhaphy, intramuscular injections in the caudal thigh and, less commonly, with neoplasia. It can also be seen following total hip replacement or acetabular fracture stabilization. These are usually neurapraxic injuries as a result of surgical retraction or thermal damage from bone cement.

Clinical presentation

Affected animals may present with lameness or LMN paresis. Lesions at, or proximal to, the lumbosacral trunk lead to complete loss of sciatic function. Affected animals are unable to extend the hip, flex the stifle or flex or extend the tarsus. Sensation is absent over digits 3, 4 and 5. Proprioceptive deficits are marked and the withdrawal reflex is weak or absent.

With lesions distal to the greater sciatic notch, gluteal function is preserved. Animals can extend their hip, although this can be difficult to appreciate clinically. For lesions distal to the greater trochanter, hamstring muscle function is maintained (biceps femoris, semimembranosus, semitendinosus). Affected animals can flex the stifle, but the limb distal to the stifle is paralysed.

In animals with fractures, segmental spinal reflexes can be difficult to assess. Cutaneous sensory testing can give an indication of neurological damage.

Management

If a neuropathy is due to impingement from an intramedullary pin, retrieval of the pin often leads to clinical improvement; additional fracture stabilization may be required. Following pelvic trauma, standard treatment of fractures should be performed, but owners should be made aware that the prognosis may be less favourable. Neurapraxia as a result of trauma will often resolve over 1–2 months; distal limb sensation is usually intact at presentation in these cases. Subsequent to an injection-associated injury, the prognosis for complete recovery may be guarded, but it depends on the degree of underlying pathology.

Regardless of the cause of the injury, extensive physiotherapy is necessary to assist with the maintenance of muscle mass and tone. The prognosis depends on the underlying cause and the severity of the nerve injury. Loss of nociception in the digits innervated by the sciatic nerve indicates a poor prognosis. Failure to recover sensory or motor function after 3 months is associated with a poor prognosis. Limb amputation may be required.

Peroneal nerve injury

Overview

Peroneal nerve injury can be associated with trauma, following surgery on the lateral aspect of the stifle or following inadvertent intraneural injection.

Clinical presentation

Clinical features include weak hock flexion and decreased sensation on the dorsal aspect of the paw. Proprioceptive deficits are often apparent.

Diagnosis

Electrophysiological studies can be helpful after 7–10 days to confirm neurological involvement and map out the area of denervation.

Management

Treatment is usually conservative. Peroneal deficits have been seen following inappropriate placement of fabellotibial sutures in the management of cranial cruciate ligament deficiency, and treatment in such cases involves removal of the offending suture.

The prognosis is variable depending on the underlying cause. Neoplasia and injuries due to inappropriate intramuscular injections are associated with a poor prognosis. Neurapraxia is more common following trauma or entrapment from a suture and carries a better outlook.

Tibial nerve injury

Overview

Tibial nerve injury is less common than peroneal nerve injury. It can be associated with trauma and intramuscular injections.

Clinical presentation

Clinical features include loss of tarsal extension, loss of sensation on the plantar aspect of the paw and proprioceptive deficits. Trophic ulceration of the plantar aspect of the paw may be observed. Differential diagnoses include Achilles tendon rupture and subtalar tarsal hyperextension.

Diagnosis

Diagnosis is usually made on clinical grounds. Electrophysiology can be useful in some cases to determine the presence of neurological abnormalities and to further map out the extent of denervation.

Management

Most cases are managed conservatively initially. Pantarsal arthrodesis may be helpful in cases that fail to improve. Complications due to trophic ulceration are not uncommon and may necessitate limb amputation. The use of orthotic devices to support the tarsus has been described (**245**).

Neuropathy secondary to intraneural injection is associated with a poor prognosis. The outlook following trauma is more variable.

Femoral nerve injury

Overview

Femoral nerve injuries are less common than sciatic nerve injuries, as the nerve is well protected within the sublumbar musculature. Femoral nerve injury can be associated with trauma, iliopsoas myopathies, retroperitoneal abscess, haematoma and neoplasia. Neurapraxia may be seen secondary to positioning of a dog in ventral recumbency with the hips extended as for perineal herniorrhaphy.



▲ 245 **Tibial nerve deficits following inappropriate intramuscular injection into the hamstring muscle group. Conscious proprioceptive deficits are evident (a) and the dog is unable to bear weight on the tarsus. The tarsus and paw are maintained in a weight-bearing position using an orthotic device (b).**

Clinical presentation

Clinical features include monoparesis with severe gait abnormality. The patient cannot bear weight on the affected limb and carries it flexed. Stifle extension and patellar reflexes are lost. Neurogenic atrophy of the quadriceps muscle rapidly develops and cutaneous sensation to the medial aspect of the limb and medial digit may be lost.

Diagnosis

Electrophysiological studies can be useful to confirm neurological involvement and determine which muscles and nerves are affected. MRI can be useful to diagnose neoplastic lesions, retroperitoneal abscesses or haematomas.

Management

Treatment is mainly supportive and consists of physiotherapy as well as measures to protect the foot from injury. Exploratory surgery to evaluate the nerve damage visually and perform neurorrhaphy (anastomosis) or neurolysis (debriding inflammatory adhesions) can be attempted in cases of severe nerve damage.

The prognosis is guarded, but depends on the severity and level of the injury with neurapraxic lesions. Lesions closest to the muscle innervated have a more favourable prognosis. If no improvement is seen within 6 months, recovery is unlikely and amputation of the affected limb should be considered.

PART 3

SPECIFIC EMERGENCIES

CHAPTER 17 Cerebrovascular accidents

CHAPTER 18 Ischaemic myelopathy

CHAPTER 19 Infectious and inflammatory diseases of the CNS

CHAPTER 20 Head trauma

CHAPTER 21 Spinal trauma

CHAPTER 22 Acute disc disease

CHAPTER 23 Status epilepticus

CHAPTER 24 Myasthenia gravis

CHAPTER 25 Tetanus and botulism

CHAPTER 26 Intracranial neoplasia and secondary pathological effects

CHAPTER 27 Metabolic encephalopathies

CHAPTER 28 Neurological toxicities

CEREBROVASCULAR ACCIDENTS

Laurent Garosi

INTRODUCTION

Cerebrovascular diseases are the underlying cause of cerebrovascular accidents (CVAs). Pathological processes that may result in cerebrovascular disease include the following:

- Occlusion of the lumen by a thrombus or embolus.
- Rupture of a blood vessel wall.
- A lesion or altered permeability of the vessel wall.
- Increased blood viscosity.

CVA, also known as stroke, is the most common clinical presentation of cerebrovascular disease. CVA is defined as a sudden onset of non-convulsive and non-progressive focal brain signs secondary to cerebrovascular disease. By convention, these signs must remain for more than 24 hours to qualify for the diagnosis of CVA, which is usually associated with permanent damage to the brain. If the clinical signs resolve within 24 hours, the episode is called a transient ischaemic attack (TIA).

CVAs are caused by an abrupt disruption of blood flow to the brain due to blockage of an artery, thus depriving brain tissue of oxygen and glucose (ischaemic stroke), or to rupture of a blood vessel, which results in haemorrhage into or around the brain (haemorrhagic stroke).

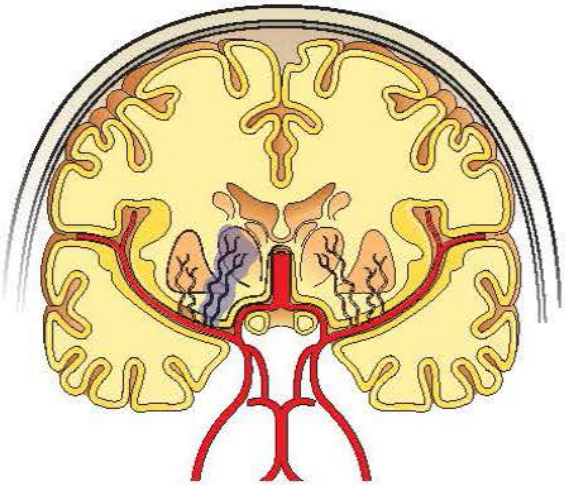
Ischaemic strokes result from occlusion of cerebral blood vessels by a thrombus or embolism. Haemorrhagic strokes result from rupture of blood vessel walls within the brain parenchyma or subarachnoid space.

AETIOLOGY AND PATHOPHYSIOLOGY

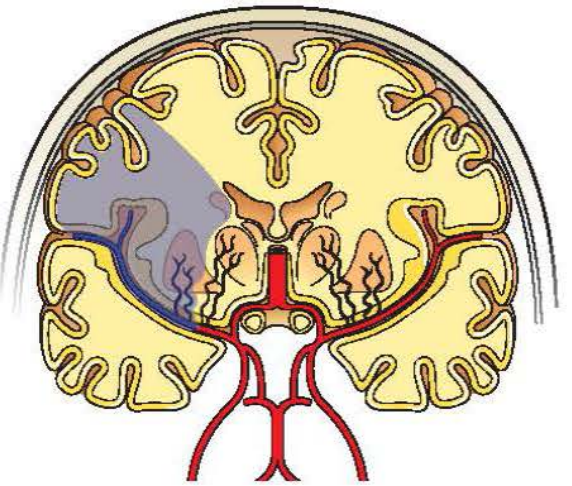
Ischaemic stroke

Ischaemic strokes have been reported infrequently in the veterinary medical literature when compared with the human medical literature. Most reports have been based on postmortem results in dogs that died or were euthanized because of the severity of the ischaemic stroke and/or the suspected underlying cause of the stroke. This may affect the putative prevalence and type of underlying causes, as it is likely that only the most severely affected dogs, or dogs in which infarction occurred secondary to a disease with a poor prognosis, would die or be euthanized. Suspected underlying causes identified in histopathologically confirmed cases include:

- Septic thromboemboli associated with bacterial endocarditis or other sources of infection.
- Atherosclerosis associated with primary hypothyroidism and Miniature Schnauzers with hypertriglyceridaemia.
- Aberrant parasite migration (*Cuterebra* spp.) or parasitic emboli (*Dirofilaria immitis*).
- Embolic metastatic tumour cells.
- Intravascular lymphoma.
- Fibrocartilaginous embolism.
- Aortic or cardiac embolism.



▲ 246 Lacunar infarct results from obstruction of a small superficial or deep perforating artery.



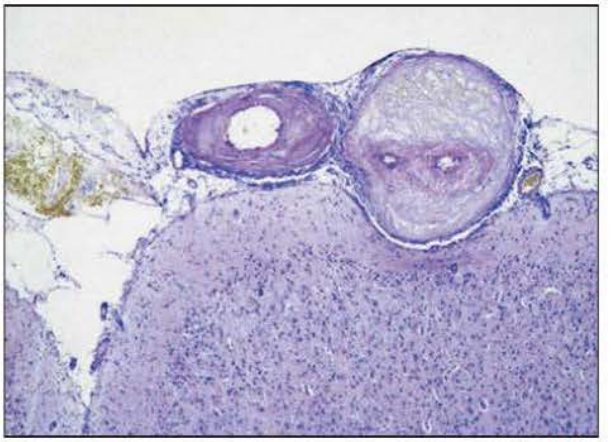
▲ 247 Territorial infarct results from obstruction of a major artery of the brain or one of its branches.

In the author's MRI-based imaging study of dogs with a brain infarct, a concurrent medical condition was detected in just over 50% of dogs. The most commonly encountered conditions were:

- Hyperadrenocorticism.
- Chronic kidney disease.
- Hypothyroidism.
- Hypertension.

Chronic kidney disease and hyperadrenocorticism were the most commonly suspected underlying causes for the hypertension. No underlying cause could be identified antemortem in nearly half of the dogs; this type of infarct of unknown origin is referred to in humans as cryptogenic. No age, sex or breed predisposition has been identified, but Cavalier King Charles Spaniels and Greyhounds appear to be overrepresented.

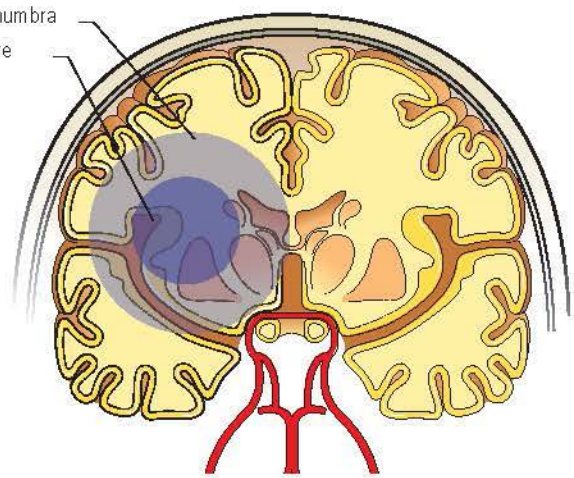
Reports of ischaemic strokes in cat are scarce. The term feline ischaemic encephalopathy has been used to describe cases of peracute onset of clinical signs consistent with a unilateral cerebral or brainstem problem caused by ischaemia. Although the cause remains unknown in most cases, some of them have been linked to *Cuterebra* spp. migration. It is believed that the migrating parasite, or the host response to it, leads to vasospasm in the cerebral vasculature (typically middle cerebral artery).



▲ 248 Severe stenosis of the middle cerebral artery secondary to an atheromatous plaque in a dog with severe hypothyroidism. (Photo courtesy Kaspar Matiasek)

With limited stores, the brain relies on a permanent supply of glucose and oxygen to maintain ionic pump function. When perfusion pressure falls to critical levels, ischaemia develops, progressing to infarction if it persists long enough and/or it is severe enough. An infarct is an area of compromised brain parenchyma caused by a focal occlusion of one or more blood vessels. It may be due either to vascular obstruction that develops within the occluded vessels (thrombosis) or to obstructive material that originates from another vascular bed and travels to the brain (thromboembolism). Depending on the size of vessel involved, infarcts can be seen as being the consequence of small vessel disease (i.e. superficial or deep perforating arteries), which gives rise to a lacunar infarct (**246**), or of large vessel disease (i.e. a major artery of the brain or its main branches), which gives rise to a territorial infarct (**247, 248**).

Two distinct regions of an infarct can be distinguished: the core, where ischaemia is severe and infarction develops rapidly, and the penumbra surrounding the core, which shows a more moderate decrease of cerebral blood flow (CBF) and allows longer durations of ischaemic stress to be tolerated (**249**). The relative volume of these two pathological regions changes as the infarct evolves. The factors causing evolution of the penumbra to irreversible injury are multiple and complex. The time window during which the penumbra is no longer viable depends on the degree of blood flow reduction, the region of the brain involved and the individual. In the penumbra, neurons are still viable, but are at risk of becoming irreversibly injured. Tissue within the penumbra has the potential for recovery and therefore is the target for interventional therapy in cases of acute ischaemic stroke. At the cellular level, the ischaemic neuron becomes depolarized as ATP is depleted and the Na^+/K^+ ATP pump, along with other ionic membrane pumps, fails leading to loss of fluid–electrolyte homeostasis. This leads to loss of ionic gradients and a net translocation of water from the extracellular to the intracellular compartment, causing cells to begin swelling (cytotoxic oedema). Over time, the ischaemic cascade progresses, with cell lysis, increased macrophage activity and disruption of the blood–brain barrier leading to the development of vasogenic oedema. This type of oedema typically takes between 4–6 hours to develop once blood flow decreases to critical ischaemic levels and may continue to progress over 24–48 hours.



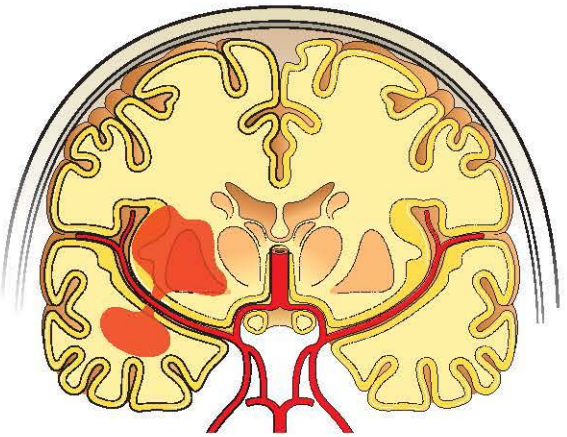
▲ **249** **In contrast to the core, where ischaemia is severe and infarction develops rapidly, areas surrounding the core (called the penumbra) show a more moderate decrease in cerebral blood flow and can tolerate longer durations of ischaemic stress. In the penumbra neurons are still viable, but at risk of becoming irreversibly injured.**

Haemorrhagic stroke

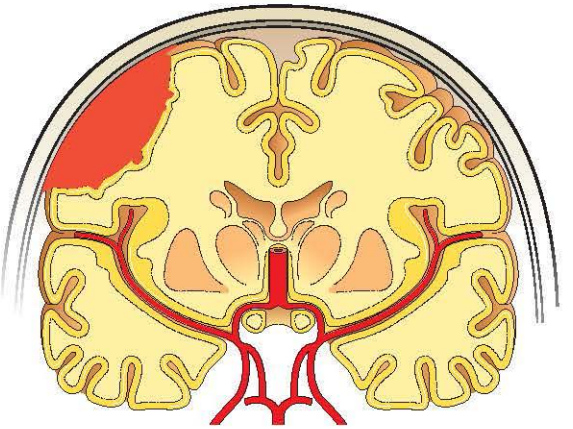
In contrast to the high incidence in man, intracerebral haemorrhage resulting from spontaneous rupture of vessels is considered rare in dogs. Secondary haemorrhage has been reported in dogs in association with:

- Rupture of congenital vascular abnormalities.
- Primary and secondary brain tumours.
- Inflammatory disease of the arteries and veins (vasculitis).
- Intravascular lymphoma.
- Brain infarction (haemorrhagic infarction).
- Impaired coagulation.

Non-traumatic subarachnoid haemorrhage has been reported in dogs, but remains very rare when compared with its occurrence in man, where aneurysmal rupture is the most common underlying cause.



▲ 250 **Intraparenchymal haematoma.**



▲ 251 **Subdural haematoma.**

In haemorrhagic stroke, blood leaks directly into the brain, forming a haematoma within the brain parenchyma (**250**), or into the subarachnoid or subdural space (**251**), leading to physical disruption of the tissue and pressure on the surrounding brain. This alters CNS volume/ pressure relationships, with the possibility of increasing ICP and decreasing CBF. As a haematoma develops, ICP may remain constant due to a system of compensation. Within the skull, a change in the volume of one intracranial constituent (brain tissue, arterial blood, venous blood and CSF) will be balanced by a compensatory change in another. This is the basis of the Monro–Kellie doctrine (see Chapter 20), which explains why some animals with large intracranial bleeds may develop substantial increases in ICP at the time of herniation. Exhaustion of the compensating mechanisms for an intracranial space-occupying lesion results in further increases in the volume of the haematoma, producing massive elevations in ICP. Due to mechanical autoregulation, CBF remains constant even though CPP may vary between 40 and 120 mmHg. The normal autoregulation of CBF may be impaired following CVAs, causing blood flow to damaged regions to become directly dependent on systemic BP. Such animals may be unable to compensate for reductions in MAP, causing decreased CPP in the presence of increased ICP. This emphasizes the importance of maintaining systemic BP. In these circumstances, systemic hypotension can result in inadequate perfusion of the brain, which leads to cerebral ischaemic and secondary neuronal injury.

CLINICAL PRESENTATION

Neurological signs seen in stroke patients are characteristically peracute or acute in onset and non-progressive or regressive in their evolution. Initially, deficits observed are usually focal, often asymmetrical and ultimately related to the area of the brain involved.

In all forms of stroke (ischaemic or haemorrhagic) the dominating feature is the temporal profile of neurological events. It is the abruptness with which the neurological deficits develop that is highly suggestive of a vascular disorder. This is then followed by an arrest and then regression of the neurological deficit in all except fatal strokes. Worsening of oedema (associated with the secondary injury phenomena) can result in progression of neurological signs for a short period of 24–72 hours. Intracranial haemorrhage can be an exception to this description, presenting with a more progressive onset over a very short period of time. Clinical signs usually regress after 24–72 hours. This is attributable to diminution of the mass effect secondary to the haemorrhage and reorganization or oedema resorption.

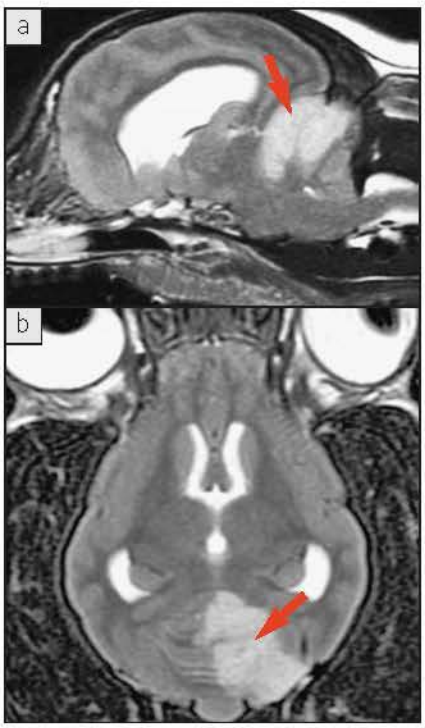
Neurological deficits usually refer to a focal anatomical diagnosis and depend on the neurolocalization of the vascular insult (telencephalon, thalamus, midbrain, pons, medulla, cerebellum). Infarction of an individual brain region is associated with specific clinical signs that reflect the loss of function of that specific region. With haemorrhagic stroke, the total clinical picture is different, as the haemorrhage usually involves the territory of more than

one artery and pressure effects cause secondary signs. Neurological signs are largely related to elevated ICP, which gives rise to non-specific signs of forebrain, brainstem or cerebellar disturbance.

Fundus examination should be considered in all animals and may reveal changes such as the presence of tortuous vessels (suggestive of systemic hypertension), haemorrhage (suggestive of coagulopathy or systemic hypertension) or papilloedema (suggestive of elevated ICP).

DIFFERENTIAL DIAGNOSIS

Head trauma; decompensation from primary or metastatic brain tumour; infectious and non-infectious encephalitis; neurotoxicity.



▲ **252** Sagittal (a) and transverse T2-weighted (b) MR images of the brain showing a cerebellar territorial infarct (arrows) in the vascular territory of the rostral cerebellar artery. The sharp demarcation, lack of mass effect and grey matter involvement are typical of an infarct.

DIAGNOSIS

Imaging studies of the brain (CT, conventional and functional MRI) are necessary to confirm stroke, define both the vascular territory involved and the extent of the lesion, as well as distinguish between ischaemic and haemorrhagic disease. Imaging studies are also necessary to rule out other causes of neurological deficit such as tumour, head trauma and encephalitis.

Ischaemic stroke

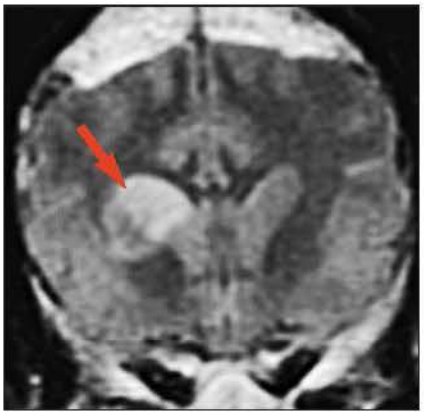
Computed tomography

CT images are frequently normal during the acute phase of ischaemia, therefore the diagnosis of ischaemic stroke using CT relies on exclusion of the clinical mimics of stroke. Early CT signs of ischaemia can be subtle and difficult to detect even by very experienced clinicians and include parenchymal hypodensity, loss of grey-white matter differentiation, subtle effacement of the cortical sulci and local mass effect.

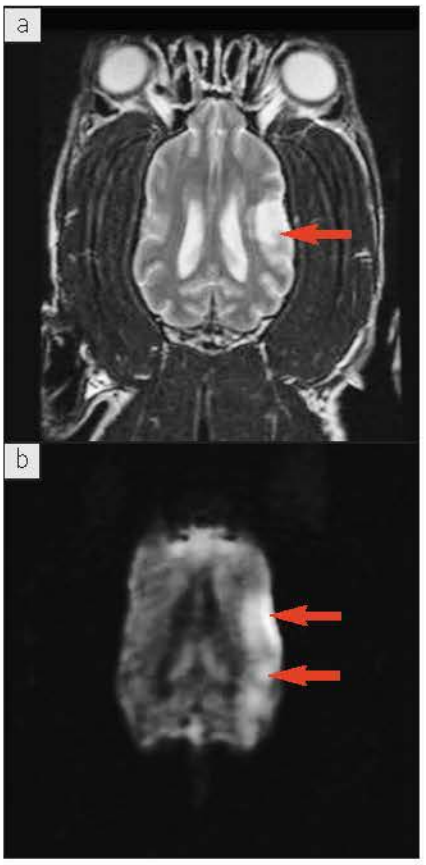
Conventional magnetic resonance imaging

Conventional MRI can be used to depict ischaemic stroke within 12–24 hours of the onset and to distinguish haemorrhagic lesions from infarction. T2-weighted and FLAIR images are particularly useful for imaging ischaemic stroke. They give a more anatomical image of the brain and depict oedema, old infarcts, microangiopathic changes, tumours and other pathology. With these sequences, ischaemic infarction appears as a hyperintense lesion. Differentiation of ischaemic core from penumbral tissue is, however, not possible. T2*-weighted (gradient echo) images are used to show the presence of, or exclude, intracranial haemorrhage. Although infarcts can sometimes be difficult to differentiate from other pathological processes such as inflammatory diseases, they tend to have certain distinguishing characteristics on conventional MR images (**252–254**).

The conformity of an infarct to a vascular territory is an important element in the diagnosis and helps in distinguishing these lesions from brain tumours, inflammation and trauma. Ischaemia/infarcts are caused by occlusion of a cerebral blood vessel. They therefore occur in and are limited to the region of the brain vascularized by the affected vessel, with resultant borders sharply demarcated from the surrounding normal brain tissue and minimal to no mass effect.



▲ **253** Transverse T2-FLAIR MR image of the brain showing a telencephalic lacunar infarct in the vascular territory of the striate arteries at the level of the caudate nucleus (arrow). Compared with the standard T2-weighted image, FLAIR images suppress the signal from cerebrospinal fluid and may allow better visualization of a periventricular lesion, as seen in this dog.



Infarcts are caused by blood perfusion failure and, therefore, energy depletion. The consequence for the cell is failure of the Na^+/K^+ pump and accumulation of Na^+ and water within the cell (i.e. cytotoxic oedema). The MRI changes seen in ischaemic parenchyma rely on an increase in tissue water content. Gradually, the T2-weighted or FLAIR images (**253**) become more hyperintense in the ischaemic region, particularly over the first 24 hours (i.e. T2 prolongation, which produces higher signal intensity in areas of increased tissue water content).

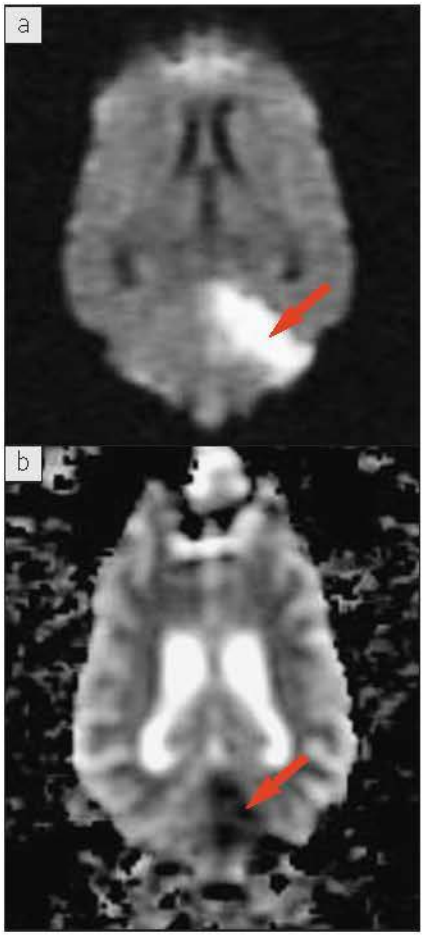
MRI changes are best appreciated in the grey matter and are well visualized in deep grey matter structures, such as the thalamus and basal nuclei, due to their selective vulnerability to ischaemia. Contrast enhancement (associated with reperfusion) is not usually seen until at least 7–10 days.

Functional magnetic resonance imaging

Functional MRI techniques have been developed for the early diagnosis of stroke in, and follow-up stroke treatment of, humans. These techniques include diffusion and perfusion imaging and magnetic resonance angiography (MRA). Diffusion and perfusion MRI are new techniques that monitor water transport in the microenvironment at cellular or capillary level. They provide complementary information about the pathophysiological processes following cerebral ischaemia.

DWI is used commonly in humans to improve the sensitivity and specificity for the diagnosis of acute stroke, making it an ideal sequence for positive identification of hyperacute stroke and excluding the clinical mimics of stroke (**254, 255**). The temporal evolution of the DWI signal also allows discrimination of acute versus chronic lesions.

◀ **254** Dorsal T2-weighted (a) and DW (b) MR images of the brain of a dog with a territorial telencephalic infarct in the vascular territory of the middle cerebral artery. DW images allow earlier detection of infarction. The lesion on this dog appears more extensive on the DW image (b) (arrows) compared with the T2-weighted image (a). Acute infarction results in water trapping within the cells and causes reduced diffusion. This phenomenon of decreased diffusion and cytotoxic oedema produces a regional hyperintensity on DWI.



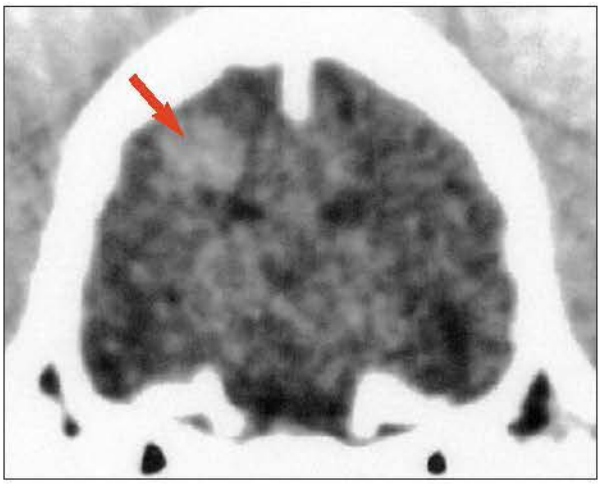
▶ 255 **Dorsal DW image (a) and apparent diffusion coefficient (ADC) map (b) of a dog with a cerebellar territorial infarct. Hyperintense lesions within the cerebellum by DWI may be attributable to restricted diffusion or artefactual due to 'T2 shine through'. To differentiate between true restricted diffusion and 'T2 shine through', bright lesions on DWI should always be confirmed with ADC maps, which exclusively measure diffusion. The ADC map helps to remove the effect of T2-weighted hyperintensity (associated with cytotoxic oedema), which can contribute to DW hyperintensity. The classic appearance of acute infarction is hyperintensity on DWI and reduced ADC.**

In addition to DWI, MR perfusion-weighted imaging is employed to depict regions of hypoperfusion in the brain and can document tissue 'at risk' (i.e. penumbra) by comparing the results with the findings on DWI.

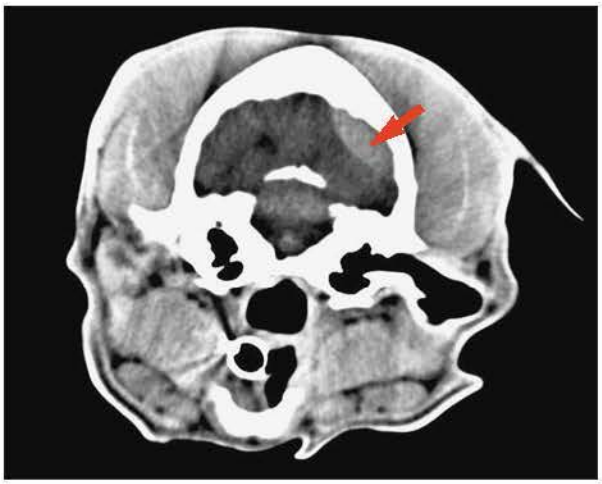
In addition to its use for tissue evaluation, MRA can non-invasively assess the intracranial vascular status of stroke patients (**256**). Two techniques can be used: time of flight MRA and contrast-enhanced MRA. One of the main limitations of MRA is its lower resolution compared with conventional angiography. This limitation becomes progressively worse as the luminal size of the vessels decreases. In humans, angiographic techniques are especially used for screening of carotid artery stenosis, vascular malformations (e.g. arteriovenous malformation, venous angioma) and aneurysms. The use of MRA in dogs has been described and may allow identification of underlying vascular lesions in cases of canine stroke.



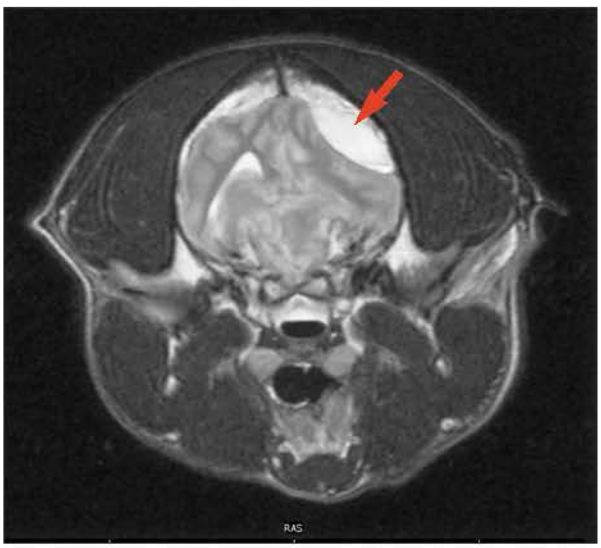
▶256 **Time-of-flight magnetic resonance angiography of the carotid arteries.**



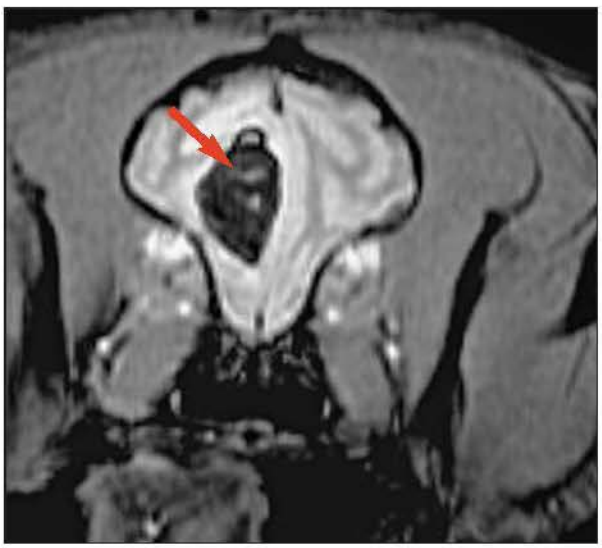
▲ 257 Transverse CT scan of the brain of a dog with intraparenchymal haemorrhage (arrow) within the right parietal lobe. Acute haemorrhage is evident as hyperdensity on CT due to the hyperattenuation of x-rays by the globin portion of haemoglobin.



▲ 258 Transverse CT scan of the brain of a dog with subdural haemorrhage at the level of the left occipital lobe (arrow) secondary to *Angiostrongylus vasorum* infestation.



▲ 259 Transverse T2-weighted MR image of the brain of a dog with subdural haemorrhage (arrow). As the haematoma ages, oxyhaemoglobin in blood breaks down sequentially into several paramagnetic products: first deoxyhaemoglobin (1–3 days), followed by methaemoglobin (3–14 days). These each have different MR signal intensities. Compared with oxyhaemoglobin and deoxyhaemoglobin, methaemoglobin appears as hyperintense on T1-weighted images.



▲ 260 Transverse T2*-gradient echo MR image of the brain of a dog with intraparenchymal haemorrhage (arrow).

Haemorrhagic stroke

Computed tomography

CT is exquisitely sensitive for the detection of acute haemorrhage. Acute haemorrhage is evident as a hyperdensity on CT due to hyperattenuation of x-rays by the globin portion of blood (**257, 258**). The attenuation decreases until the haematoma is isodense at about 1 month after the onset. The periphery of the haematoma contrast enhances from 6 days to 6 weeks after the onset, due to revascularization.

Conventional magnetic resonance imaging

The MR signal intensity of intracranial haemorrhage is influenced by several intrinsic (time from ictus, source, size and location of haemorrhage) and extrinsic (pulse sequence and field strength) factors (**259**). The causes of these variations in haematoma intensity are difficult to evaluate with clinical studies since it is frequently impossible to ascertain precisely the interval between haemorrhage and MR imaging. As the haematoma ages, oxyhaemoglobin in blood sequentially breaks down into several paramagnetic products: first deoxyhaemoglobin, followed by methaemoglobin and, finally, haemosiderin.

The two most important biophysical properties in the generation of MR signal intensity patterns seen in evolving intracranial haematomas are: (1) the paramagnetic effects of iron associated with the changing oxygenation states of haemoglobin, and (2) the integrity of red blood cell membranes that, when intact, compartmentalize the paramagnetic iron.

The earliest possible detection of haemorrhage depends on the conversion of oxyhaemoglobin to deoxyhaemoglobin, which is believed to occur after the first 12–24 hours. In contrast to oxyhaemoglobin, where iron is shielded from surrounding water molecules, resulting in an MR signal similar to that of normal brain parenchyma, the iron exposed to surrounding water molecules in the form of deoxyhaemoglobin creates a signal loss, making it easy to identify on T2-weighted and susceptibility-weighted sequences. Gradient echo sequences have proven to be the most accurate of all of the MR pulse sequences, and more accurate than CT, in predicting the extent of haemorrhage on pathological examination in a dog model. Compared with other sequences, gradient echo scans demonstrate readily detectable hypointensity regardless of the time from ictus, the source and location of haemorrhage or the field strength (**260**). Due to the progressive centripetal increase in the deoxyhaemoglobin concentration, the periphery of the haematoma is often initially more hypointense on susceptibility-weighted images than on T2-W images. Hypointensities on gradient echo images are, however, not specific for haemorrhage and may also be seen with calcification, air, iron, foreign bodies and melanin. However, air, calcification and often foreign bodies would also normally be hypointense on all the pulse sequences.

Cerebrospinal fluid analysis

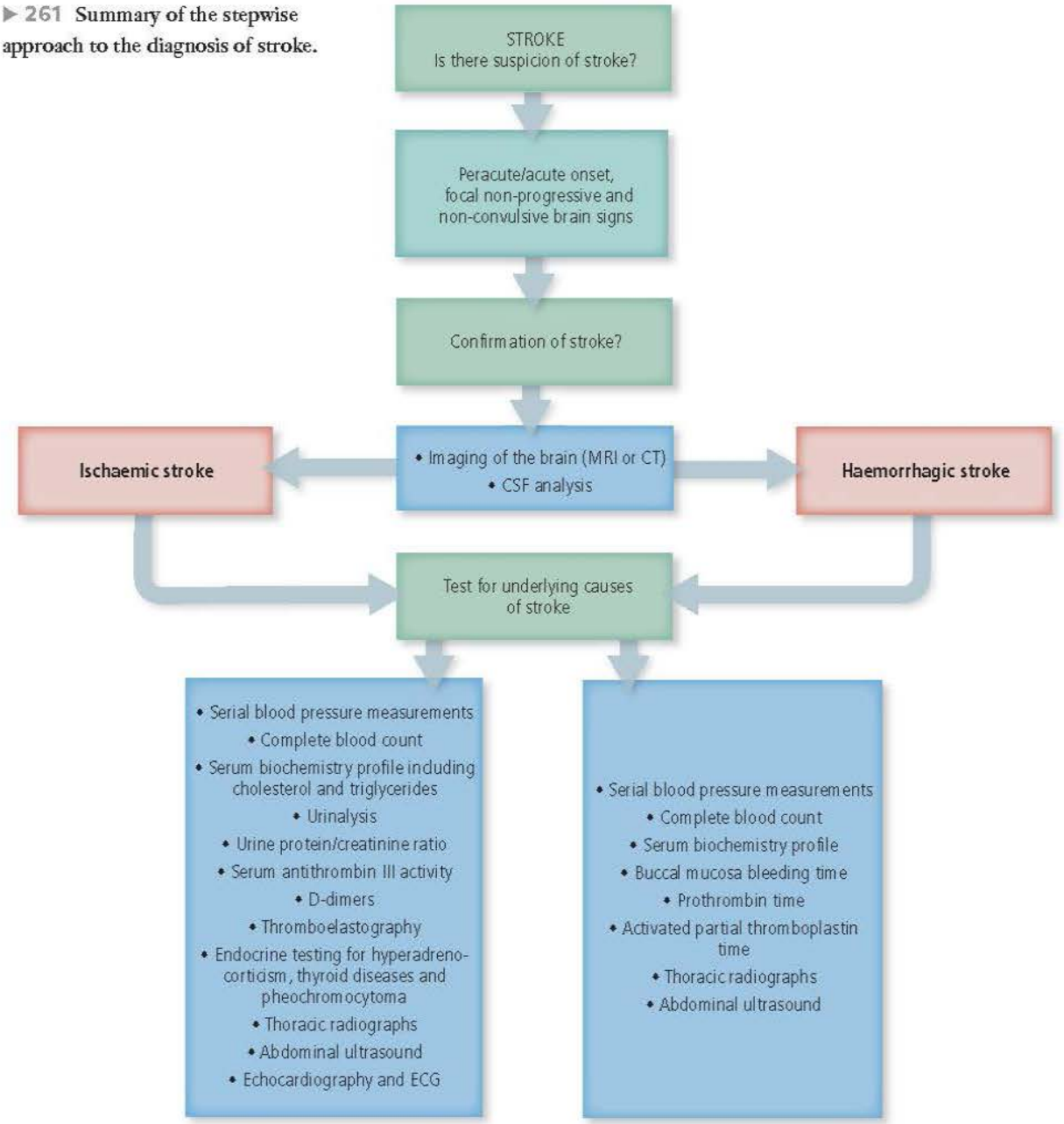
CSF analysis is unlikely to confirm a diagnosis of CVA, but may help to rule out inflammatory CNS disease. CSF is variable in dogs and cats with CVA. In most cases it is either normal or reflects a mild mononuclear or neutrophilic pleocytosis. CSF proteins are occasionally elevated.

IDENTIFICATION OF UNDERLYING CAUSES OF STROKE

In the case of presumptive or confirmed ischaemic stroke, ancillary diagnostic tests should focus on evaluating the animal for hypertension (and its potential underlying causes), endocrine disease (hyperadrenocorticism, hypothyroidism, hyperthyroidism, diabetes mellitus), kidney disease (especially protein-losing nephropathy), heart disease and metastatic disease (**261**, next page).

Diagnostic tests in presumptive or confirmed cases of haemorrhagic stroke should focus on screening the animal for a coagulopathy or hypertension (and potential underlying causes) as well as metastatic disease (particularly haemangiosarcoma).

▶ **261** **Summary of the stepwise approach to the diagnosis of stroke.**



TREATMENT

Once the diagnosis of a stroke has been made (**261**), any potential underlying or associated disease should be identified and treated. Generally, treatment of these patients aims to provide supportive care, maintain adequate tissue oxygenation and manage neurological and non-neurological complications. Nursing management of a recumbent dog will be vital to the success of more specific therapies. Such management includes attention to the prevention of decubital ulceration, aspiration pneumonia and urine scald, in addition to physical therapy and enteral nutrition provision. More specific therapies are aimed at preventing further neurological deterioration.

Ischaemic stroke

Most cases of ischaemic stroke recover within several weeks with only supportive care. Potential underlying causes should be investigated and treated accordingly to limit the risk of recurrence (**262**).

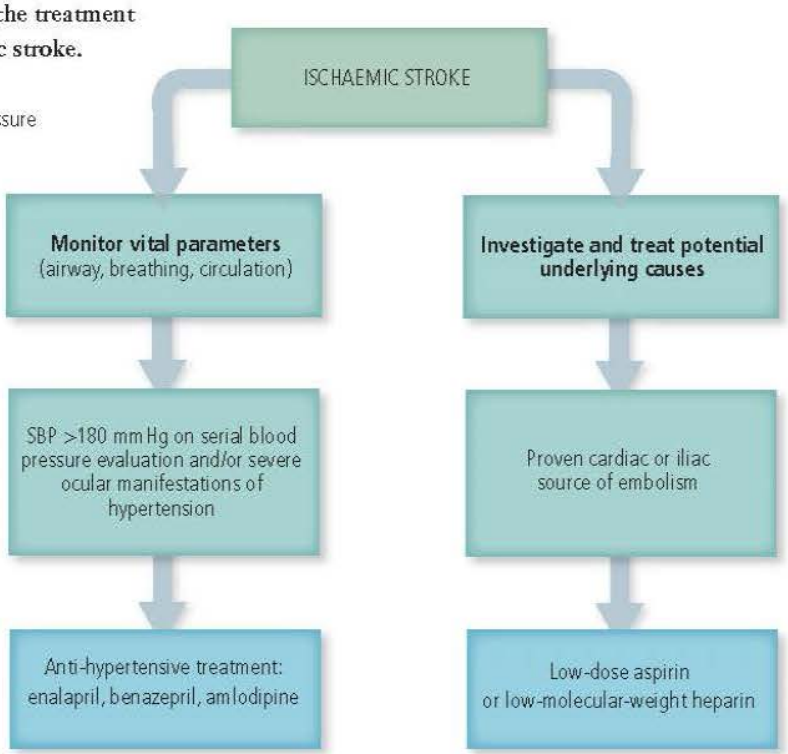
Treatment revolves around three principles: (1) monitoring and correction of basic physiological variables (e.g. oxygen level, fluid balance, BP, body temperature); (2) inhibition of the biochemical and metabolic cascades subsequent to ischaemia to prevent neuronal death (the concept of neuroprotection); and (3) restoration or improvement of CBF by thrombolysis in the presence of a thrombus. The potentially salvageable portion of the ischaemic zone (ischaemic penumbra) is the presumed therapeutic target for both thrombolytic and neuroprotective stroke therapy. The time period during which injury may be reversible is called the therapeutic window. It is estimated that this 'window of opportunity' is approximately 6 hours before irreversible neurological damage occurs.

Monitoring and correction of basic physiological variables

Fortunately, the vast majority of ischaemic stroke patients have no major difficulty maintaining their airways, breathing efforts or circulatory competence early in their clinical course. Some controversies exist surrounding the management of hypertension in the setting of an ongoing acute ischaemic stroke. As well as being a potential risk factor, hypertension can occur as a physiological response to a stroke to ensure an adequate CPP in the penumbra of the infarct for up to 72 hours after onset. Maintenance of systemic arterial BP within the physiological range is essential, and aggressive lowering of BP should be avoided during the acute stages unless the patient is at a high risk of end-stage organ damage (systolic BP remaining >180 mmHg). In such cases, hypertension can often be controlled with an ACE inhibitor such as enalapril (0.25–0.5 mg/kg q12h) or benazepril (0.25–0.5 mg/kg q12h) and/or calcium channel blockers such as amlodipine (0.1–0.25 mg/kg q24h), which tend to be more effective.

▶ 262 Summary of the treatment approach to ischaemic stroke.

SBP = systemic blood pressure



Neuroprotection

There is no evidence that glucocorticoid treatment provides any beneficial neuroprotection in cases of stroke. Aside from the lack of proven benefit in veterinary stroke patients, the use of glucocorticoids may increase the risk of gastrointestinal complications and infection. Treatment strategies for ischaemic stroke considered in man, utilizing other neuroprotective agents (N-methyl-D-aspartate antagonists, Ca^{2+} channel blockers, sodium channel modulators) or anti-platelet and thrombolytic therapy, remain to be evaluated clinically in dogs. Although some of the neuroprotective agents have resulted in a dramatic decrease in the size of stroke lesions in experimental animal models, these agents either have failed to prove their efficacy in clinical trials or are awaiting further investigation.

Thrombolytic therapy

At the time of writing, there are no definitive data in humans or animals to confirm a significant improvement in clinical outcome in patients with acute ischaemic stroke treated with unfractionated heparin as thrombolytic therapy. Despite conflicting results regarding its efficacy, intravenous recombinant tissue plasminogen activator is sometimes used in human stroke patients if it can be given within the first 3 hours. This critical time window makes the use of thrombolytic treatment unrealistic in veterinary neurology. Furthermore, this type of treatment carries a significant risk of intracranial haemorrhage following treatment. Anti-platelet therapy with low-dose aspirin (0.5 mg/kg PO q24h) or clopidogrel (2–4 mg/kg PO q24h) can be used prophylactically to prevent clot formation in proven cardiac sources of an embolus.

Haemorrhagic stroke

The most important consideration in haemorrhagic stroke is maintenance of cerebral perfusion by treatment of hypotension and elevated ICP, as well as treating the underlying cause if one has been identified (**263**).

The medical management of dogs with intracranial haemorrhage commonly includes: (1) stabilization of the patient (airway protection, monitoring and correction of vital signs); (2) assessment and monitoring of the neurological status; (3) determination and treatment of potential underlying causes of the haemorrhage; and (4) assessment of the need for specific treatment measures including management of raised ICP. The risk of neurological deterioration and cardiovascular instability is highest during the first 24 hours after the onset of an intracranial haemorrhage, as the space-occupying lesion slowly expands and cerebral vasogenic oedema develops. The initial approach to treatment of the animal with haemorrhagic stroke should focus on extracranial stabilization, closely followed by therapies directed towards intracranial stabilization and treatment of the potential underlying cause if one is identified. Careful monitoring is essential during the initial period and should include assessment of vital parameters as well as the neurological status.

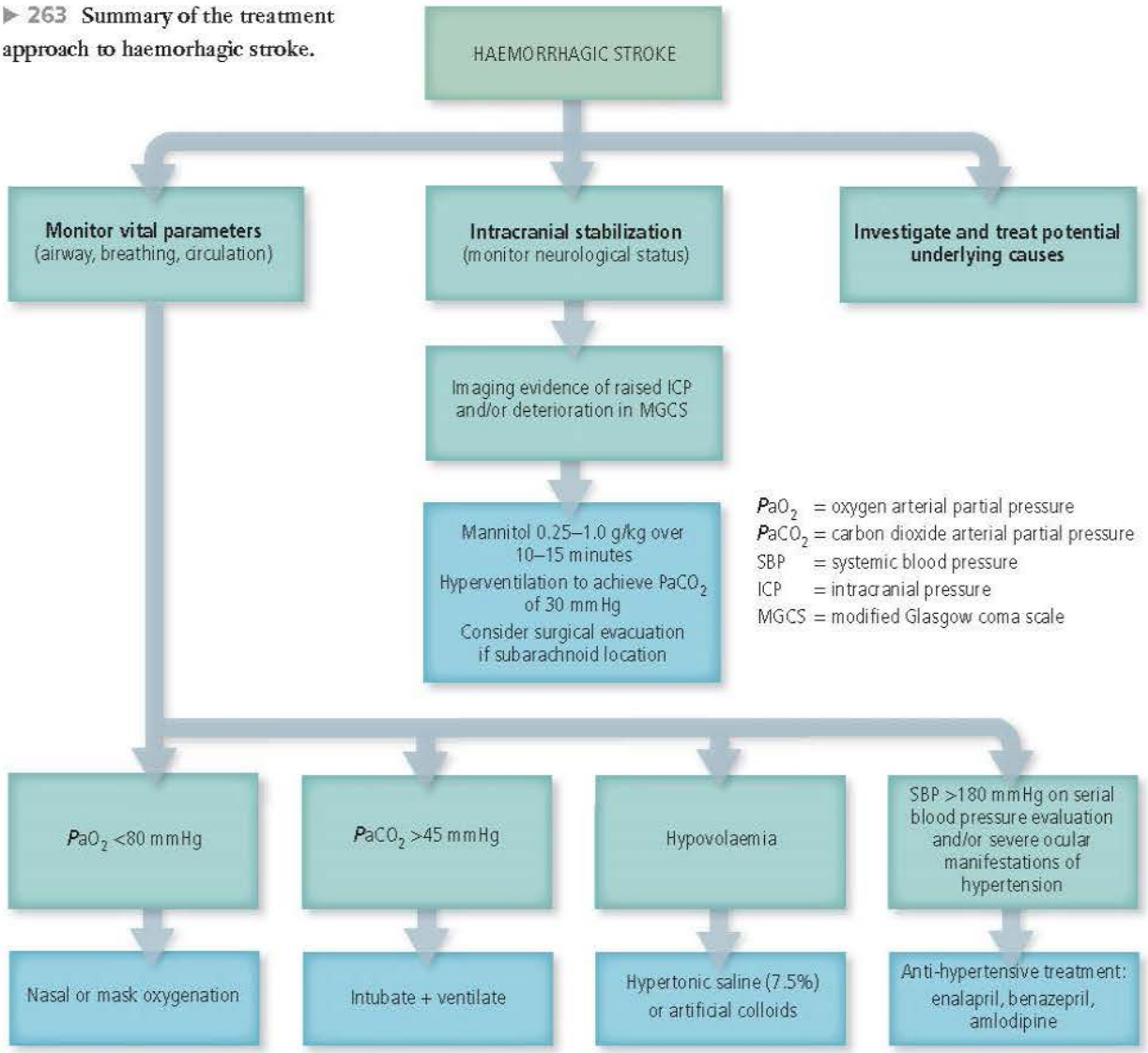
Extracranial stabilization

Extracranial stabilization involves careful monitoring of vital parameters (e.g. oxygen levels, fluid balance, BP, body temperature) and correction of any deviation from normal. As with any other intracranial disease, hypoxia should be avoided, but there is no evidence in humans to support the routine use of oxygen for the treatment of haemorrhagic stroke, in the absence of hypoxia.

Hypoventilation may occur as a result of damage to the respiratory centre in the brainstem following raised ICP in the caudal fossa. The impaired respiratory drive results in elevation in $PaCO_2$ and resultant vasodilation, which in turn aggravate intracranial hypertension. $PaCO_2$ should be maintained within a normal range and not allowed to exceed 40 mm Hg. Immediate intubation and ventilation should be considered if $PaCO_2$ cannot be maintained within an acceptable range.

The correction of tissue perfusion is an important stabilizing therapy in any patient with haemorrhagic stroke. The primary goal of fluid therapy is rapid restoration of BP, such that CPP is maintained at

▶ **263** **Summary of the treatment approach to haemorhagic stroke.**



>70 mm Hg. Hypovolaemia should be recognized and treated with volume expansion, preferably using artificial colloids or hypertonic saline (7.5%) to achieve rapid restoration of blood volume and pressure while limiting the volume of fluid administered. Hypertonic saline has many properties that may make it a superior rescuitation fluid for patients with intracranial disease such as haemorrhagic stroke. The recommended dose of 7.5% sodium chloride for volume expansion is 2–4 ml/kg (cats) and 4–6 ml/kg (dogs) given over 5–10 minutes. The use of glucose-containing solutions is discouraged as hyperglycaemia has been shown to correlate with poor outcome in human stroke patients. As such, blood glucose levels should be monitored from the time of presentation. Hypotonic fluid should also be avoided.

As with ischaemic stroke, attempts to lower and normalize BP should be reserved for animals at a high risk of end-stage organ damage (systolic BP remaining >180 mmHg) and/or animals with severe ocular manifestations of hypertension such as retinal detachment or intraocular haemorrhage. However, moderate levels of hypertension should not be treated, as systemic hypertension may be secondary to the intense reflex sympathetic response to intracranial hypertension, which is a compensatory mechanism to maintain cerebral perfusion. Treatment recommendations for lowering BP are detailed in the section on treatment of ischaemic stroke.

Intracranial stabilization

Once initial assessment and extracranial stabilization have occurred, medical intervention to address intracranial issues should be considered, with the main focus being on decreasing ICP. Three principles can be applied: (1) reducing cerebral oedema associated with intracranial haemorrhage; (2) optimizing cerebral blood volume; and (3) eliminating the space-occupying mass.

Osmotic diuretics, such as mannitol, are very useful for treating cerebral oedema and resultant intracranial hypertension associated with pathologies such as head trauma, brain tumours and encephalitis. There is insubstantial evidence to suggest that mannitol exacerbates intracranial haemorrhage, therefore osmotic diuretics are routinely used in the control of ICP in human patients with known intracranial haemorrhage. Mannitol therapy (0.25–2.0 g/kg IV over 10–20 minutes up to q4–8h) may be initiated to treat suspected elevated ICP secondary to haemorrhagic stroke. Mannitol's main effect is to enhance CBF by reducing blood viscosity. It should, however, be avoided in hypovolaemic patients.

Cerebral blood volume is another intracranial component that contributes to ICP. In a rapidly deteriorating animal, hyperventilation can temporarily be used to reduce ICP. The aim of hyperventilation is to reduce cerebral blood volume, and hence ICP, by causing a hypocapnic vasoconstriction. However, excessive hyperventilation can be accompanied by a reduction in global CBF, which may drop below ischaemic thresholds. Therefore, it is not a recommended therapy unless the $PaCO_2$ can be closely monitored with capnography or arterial blood gas analysis.

Elimination of the space-occupying mass within the cranial vault is the third method by which ICP reduction can be obtained. Surgical evacuation of the haematoma can therefore be employed in dogs with large haematomas (mostly subarachnoid) and a deteriorating neurological status.

PROGNOSIS

The prognosis for ischaemic or haemorrhagic stroke depends overall on the initial severity of the neurological deficit, the initial response to supportive care and the severity of the underlying cause if one has been identified. Fortunately, most cases of ischaemic stroke recover within several weeks with only supportive care. In a recent retrospective study of 33 dogs with MRI or necropsy evidence of brain infarction, there was no association between the region of the brain involved (telencephalic, thalamic/midbrain, cerebellum), the type of infarction (territorial or lacunar) and the outcome. However, dogs with a concurrent medical condition had a significantly shorter survival time than those dogs with no identifiable medical condition. Dogs with a concurrent medical condition also were significantly more likely to suffer from recurrent neurological signs due to subsequent infarcts.

ISCHAEMIC MYELOPATHY

Luisa De Risio

INTRODUCTION

Ischaemic myelopathy is a vascular disease of the spinal cord caused by embolization or, less commonly, thrombosis of spinal cord blood vessels. Vascular spasm can also occur secondary to acute traumatic events (for further details see Chapter 21). The abrupt disruption of blood flow to an area of the spinal cord results in ischaemic necrosis and associated peracute (<6 hours) or acute (6–24 hours) neurological signs, with distribution and severity referable to the site and extent of the infarction.

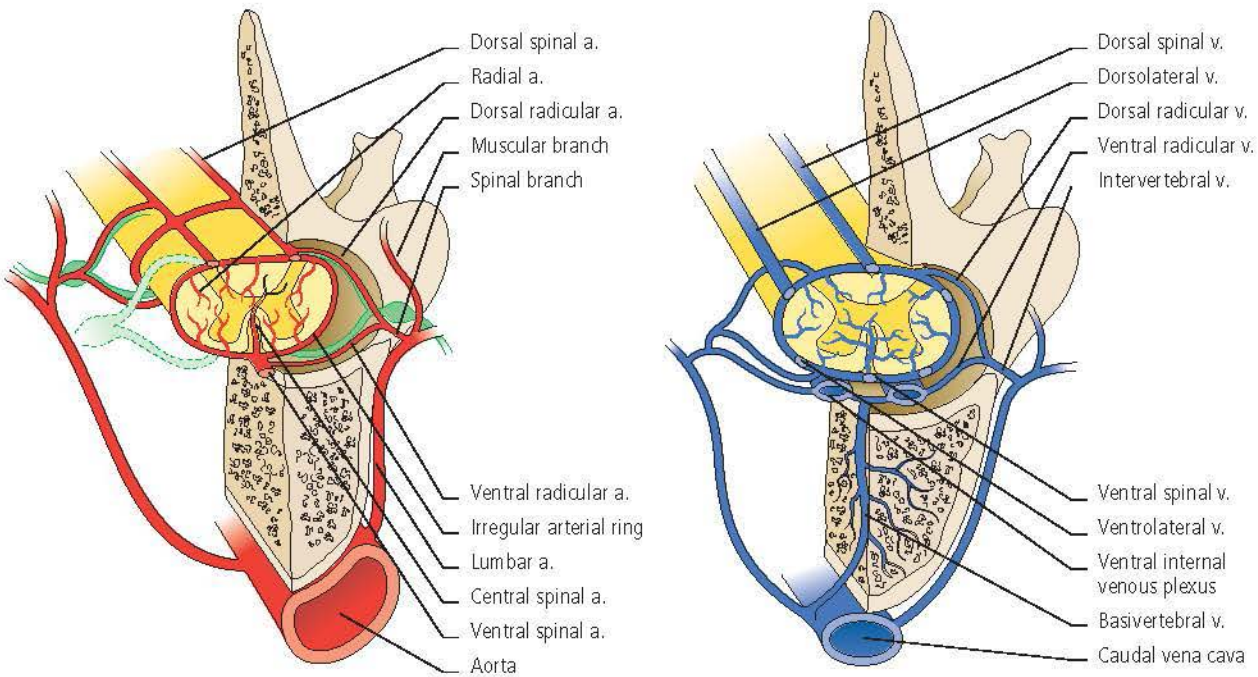
Fibrocartilaginous emboli are the most commonly documented cause of spinal blood vessel occlusion in histologically confirmed cases of ischaemic myelopathy. Hence this condition is called 'fibrocartilaginous embolism' (FCE) or 'fibrocartilaginous embolic myelopathy' (FCEM).

AETIOLOGY AND PATHOPHYSIOLOGY

The intraparenchymal (intrinsic) spinal cord arteries are functional end arteries and their occlusion leads to ischaemia of the territory supplied. The arterial and venous blood supply of the spinal cord is shown (**264**).

The most common cause of ischaemic necrosis of the spinal cord parenchyma is embolization of spinal arteries or veins, or a combination of both, by fibrocartilaginous material. Arteriovenous anastomoses have been demonstrated in the spinal cord vasculature and could explain the presence of emboli on either side of the circulation regardless of whether the entry point is arterial or venous.

▼ 264 The arterial and venous supply to the lumbar spinal cord.



Histological and histochemical studies have shown that the embolized fibrocartilage has the same collagen type as that of the intervertebral disc nucleus pulposus. The fact that this type of embolism occurs primarily in the spinal cord further supports the involvement of the nucleus pulposus as the source of the fibrocartilage. Additionally, it has been hypothesized that fibrocartilage may arise from metaplasia of the vascular endothelium, which later ruptures into the lumen and embolizes within the spinal cord vessels. Vertebral growth plates may represent the source of the fibrocartilage in immature dogs. Ischaemic myelopathy may also result from material other than fibrocartilage that obstructs the intrinsic spinal blood vessels, such as thrombi or bacterial, parasitic, neoplastic or fat emboli. Pre-existing medical conditions (e.g. cardiomyopathy, hypothyroidism, hyperthyroidism, hyperadrenocorticism, chronic renal failure, hypertension) that may predispose to embolization or thrombosis should be considered and investigated, particularly in cats.

The pathophysiology of this condition is still unclear. Several hypotheses have been proposed to explain how the fibrocartilaginous material, originating from the intervertebral disc nucleus pulposus, enters the vascular system. These include:

- Direct penetration of nucleus pulposus fragments into the spinal cord vessels or into the vertebral vessels. Extrusion of degenerated disc material into the adjacent ventral internal vertebral venous plexus has sometimes been observed during postmortem examinations. Increased intrathoracic and intra-abdominal pressure during coughing, straining, exercise or trauma (Valsalva's manoeuvre) could generate retrograde venous propulsion of the fibrocartilage into the spinal arteries.
- Mechanical herniation of nucleus pulposus into the vertebral bone marrow, with subsequent retrograde entrance into the ventral internal vertebral venous plexus.
- Presence of embryonic remnant vessels within the nucleus pulposus (which is normally avascular in adults).
- Neovascularization of the degenerated intervertebral disc. In man and non-chondrodystrophic dogs with disc degeneration, ingrowth of blood vessels within the degenerated annulus fibrosus has been documented. A sudden rise in intervertebral disc pressure exceeding arterial BP may result in penetration of nucleus pulposus fibrocartilage into the newly-formed intervertebral disc vessels (or into the embryonic remnant vessels) and progression into the intrinsic spinal cord vessels. The presence of fibrocartilage within newly-formed blood vessels in the degenerated intervertebral disc has been reported in two dogs with histologically confirmed ischaemic myelopathy.

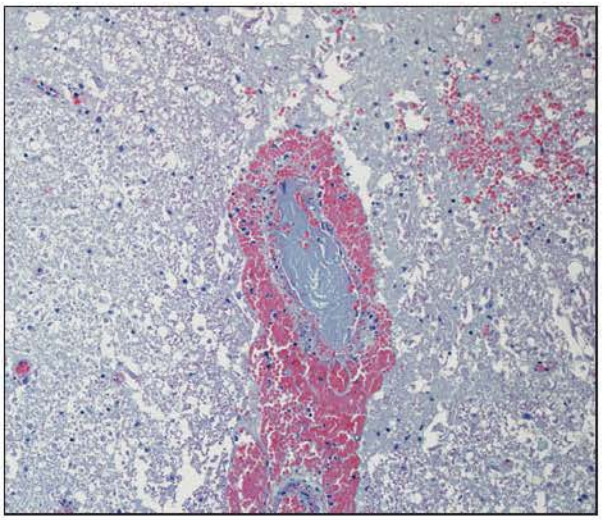
The ischaemic injury caused by the arterial obstruction initiates a series of biochemical and metabolic events (similar to the secondary injury phenomenon described in Chapter 21), which result in neuronal and glial cell death. The grey matter, due to its greater metabolic demand, is affected more severely than the white matter.

CLINICAL PRESENTATION

The typical clinical presentation is characterized by peracute (<6 hours) onset of non-painful, non-progressive (after the first 24 hours) and often asymmetric myelopathy (**265**).

Ischaemic myelopathy has been reported commonly in dogs and sporadically in several other species including cats, humans, horses, pigs, turkeys, sheep, a calf, a tiger, a tayra and a pigtail macaque. Ischaemic myelopathy due to fibrocartilaginous embolization has been reported most commonly in large breed dogs; however, this disorder has also been described in small breed dogs and, particularly, in Miniature Schnauzers. Ischaemic myelopathy is, however, very rare in chondrodystrophic breeds. Either gender can be affected, but a few studies on dogs have documented a male to female ratio of about 2.5:1.

Dogs and cats of any age can be affected. Ischaemic myelopathy has been confirmed histologically in young (8–13 weeks of age) Irish Wolfhounds of either gender (but especially males). In the author's MRI-based study on 52 dogs the median age at diagnosis was 6 years



▲ 265 Spinal cord arteriole is obstructed with pale blue material consistent with fibrocartilaginous nucleus pulposus (× 20). (Photo courtesy Victoria Watson)

(range, 3 months to 11 years and 11 months). The median age reported in other studies on dogs with histologically confirmed ischaemic myelopathy ranged from 5–6 years. Age at onset of signs in cats with ischaemic myelopathy has been reported between 4 and 12 years and the majority were Domestic Shorthair cats.

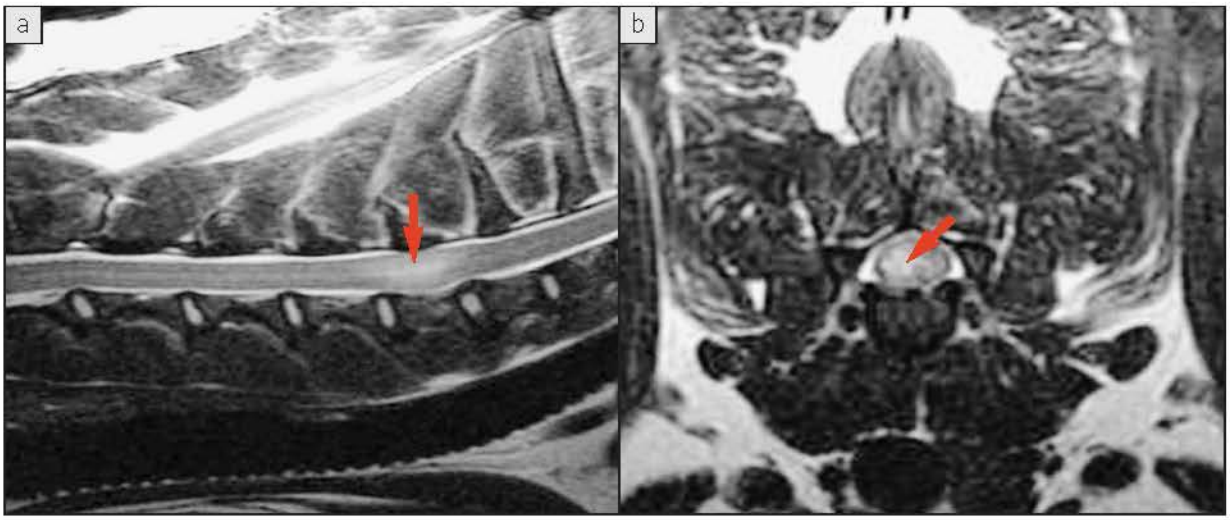
In addition to the typical clinical presentation, some dogs can show spinal hyperaesthesia at the onset of neurological signs and occasionally this can be identified at clinical examination performed within 24 hours of onset. Rarely, neurological dysfunction progresses for 48 hours due to worsening of spinal cord ischaemia, oedema and malacia (associated with secondary injury phenomenon). However, most commonly, maximal neurological deficits occur within the first 12–24 hours of disease and are followed by gradual improvement or stabilization of signs depending on the extent and severity of the ischaemic lesion. In the study of 52 dogs mentioned above, onset of neurological signs was peracute or acute (<24 hours) in all dogs. Within the first 24 hours after onset, according to the owners, neurological signs were static in 34 dogs (65%) and progressive in 18 dogs (35%).

Neurological deficits refer to the spinal cord segments involved (C1–C5, C6–T2, T3–L3 or L4–S3) and are often asymmetric. Lateralization of signs is the result of asymmetric branching of the intrinsic spinal cord vasculature, particularly of the central branches of the ventral spinal artery, and has been reported in 53–86% of dogs. The most commonly affected spinal cord segments have been reported to be L4–S3 (43–47%) and C6–T2 (30–33%) in dogs with a histologically confirmed diagnosis, and L4–S3 (44–50%) and T3–L3 (37–42%) in dogs with a presumptive diagnosis. Some dogs with ischaemic myelopathy affecting the T3–L3 spinal cord segments and causing severe motor dysfunction have been reported with decreased flexor withdrawal reflexes in the hindlimbs in the acute stages of the disease. In the author's study, three (6%) paraplegic dogs with a T3–L3 lesion on MRI had an interruption of the cutaneous trunci reflex consistent with the site of the lesion on MRI, but also exhibited a decreased flexor withdrawal reflex in the hindlimbs, a normal to increased patellar reflex, normal perineal reflex and normal nociception. It has been suggested that the transient decrease of the hindlimb flexor reflex in dogs with acute thoracolumbar spinal cord injury is due to sudden interruption of descending supraspinal input on motor neurons and interneurons, fusimotor depression and increased segmental inhibition. This phenomenon has important clinical implications, as it may lead to an erroneous neuroanatomical localization, site of diagnostic investigation and prognosis.

Rarely, multiple ischaemic lesions within different regions of the CNS have been reported following fibrocartilaginous embolization. Concurrent brainstem and spinal cord fibrocartilaginous emboli have been documented histologically in a sheep and a dog, and in humans.

DIFFERENTIAL DIAGNOSIS

Acute non-compressive nucleus pulposus extrusion; intervertebral disc extrusion; intra-/extramedullary haemorrhage (coagulopathy, trauma); infectious and non-infectious myelitis; intramedullary neoplasia.



▲ **266** (a) Mid-sagittal T2-weighted FSE image of C2–T1 vertebrae in an 8-year-old male neutered Staffordshire Bull Terrier with acute-onset right-sided tetraparesis and Horner's syndrome. The spinal cord overlying the C6 vertebral body is swollen and has a focal intramedullary hyperintensity (arrow). (b) Transverse T2-weighted FSE image through the intramedullary hyperintensity depicted in **266a**. The focal and relatively sharply demarcated intramedullary hyperintensity (arrow) involves predominantly the grey matter and is lateralized to the right.

DIAGNOSIS

The antemortem diagnosis of ischaemic myelopathy is based on the typical clinical presentation (peracute/acute non-progressive, non-painful, usually asymmetric myelopathy), exclusion of other causes of peracute/acute myelopathy (by means of myelography, CT or MRI, and CSF analysis) and visualization of a lesion compatible with spinal cord ischaemia on MRI.

Magnetic resonance imaging

MRI is the diagnostic imaging modality of choice to attain an antemortem diagnosis of ischaemic myelopathy. In addition to excluding other causes of myelopathy (similar to myelography and CT), it allows visualization of signal intensity changes suggestive of ischaemic infarction.

The MRI features suggestive of ischaemic myelopathy include (**266**):

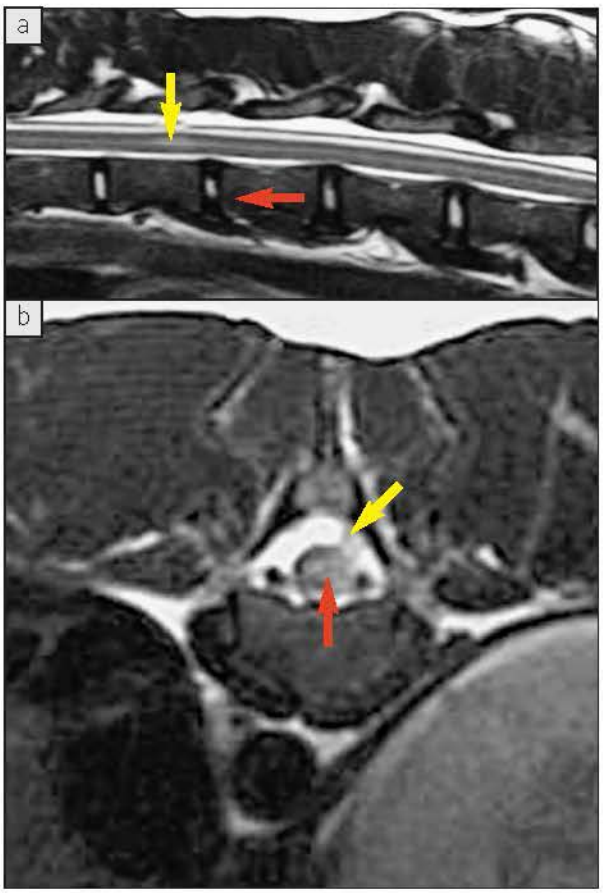
- A focal, relatively sharply demarcated intramedullary lesion (oedematous infarcted tissue), predominantly involving the grey matter that appears:
  - Hyperintense to spinal cord grey matter on T2-weighted fast spin echo (FSE) and FLAIR images and iso- or hypointense to spinal cord grey matter on T1-weighted FSE images.
  - Sometimes, contrast enhances (usually mild and heterogeneous) as early as 48 hours after onset of signs and becomes apparent by the fifth to seventh day after onset of signs.
- MRI imaging performed within 24–48 hours following onset of neurological signs may be normal.

In the human literature it is widely accepted that conventional MRI may not allow detection of the ischaemic spinal cord lesion in the first 48 hours after onset of neurological signs. Indeed, repeated MRI is commonly used in people with suspected ischaemic myelopathy. In the author's MRI-based study, 11 of 52 dogs imaged with a 1.5 Tesla MRI scanner between 12 and 72 hours (median, 12–24 hours) after onset of signs had normal MR images. In another study, ischaemic myelopathy was confirmed histologically in dogs with normal MRI performed in the acute stages of the disease. The degree of ischaemic insult, the size of the infarction and the availability of high-contrast resolution MRI influence the ability to detect signal changes during the first 24–48 hours of ischaemic myelopathy.

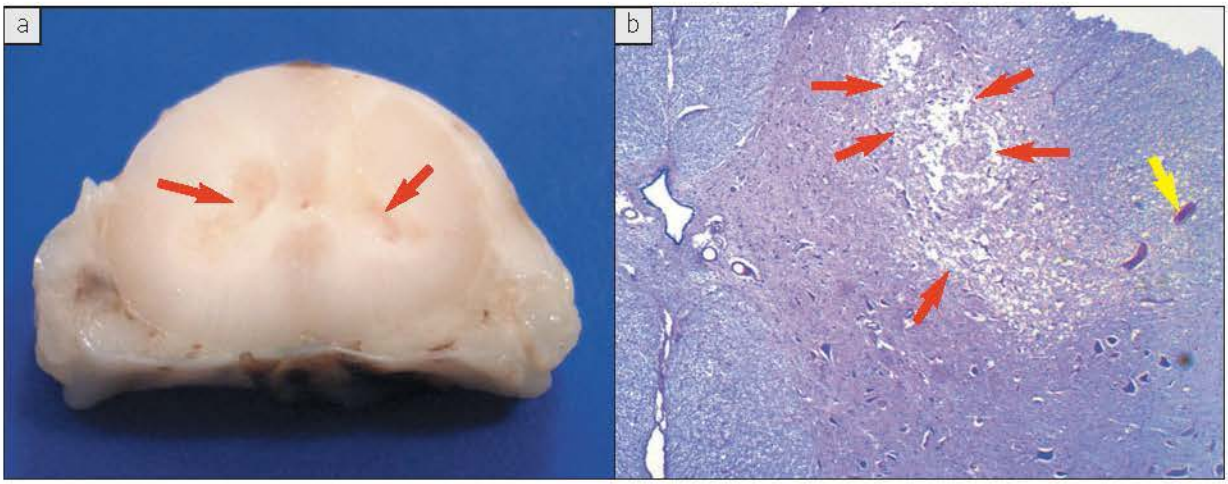
DWI is used in humans to improve the sensitivity and specificity of ischaemic myelopathy diagnosis in the acute phase of the disorder. However, in animals, DWI is technically challenging because of the relatively small size of the spinal cord, low spatial resolution and the magnetic susceptibility to artefacts caused by vascular and CSF pulsation.

MRI can help to differentiate between ischaemic myelopathy and acute non-compressive nucleus pulposus extrusion, whose clinical presentation can be very similar. The MRI findings of acute non-compressive nucleus pulposus extrusion include (**267**):

- Presence of a focal intramedullary hyperintensity overlying an intervertebral disc, with reduced volume and signal intensity of the nucleus pulposus on T2-weighted FSE images.
- Narrowed intervertebral disc space.
- Presence of extraneous material or signal change within the epidural space dorsal to the affected disc, with absent or minimal spinal cord compression.



◀ **267** (a) Mid-sagittal T2-weighted FSE image of T10–L1 vertebrae of a 3-year-old male neutered Lurcher with acute-onset left hindlimb paresis while playing. The nucleus pulposus of T11/T12 intervertebral disc (red arrow) is smaller than the nucleus pulposus of adjacent intervertebral discs. There is moderate ill-defined intramedullary hyperintensity within the spinal cord overlying the T11/T12 intervertebral disc space and caudal half of T11 vertebral body (yellow arrow). (b) Transverse T2-weighted FSE image at the level of the caudal end-plate of T11. The ill-defined intramedullary hyperintensity is worse on the left side (red arrow). Within the epidural space, dorsolaterally to the spinal cord on the left side, there is focal disruption of the epidural fat (yellow arrow) and presence of material isointense to the intervertebral disc nucleus pulposus. There is no spinal cord compression.



▲ 268 (a) Transverse section of the cervical spinal cord (C5) of an adult female mongrel dog. Note the bilaterally asymmetric cavitation/malacia of spinal grey matter (arrows). (b) Low-power field image of the cervical spinal cord transverse section showing focal disruption of the lateral and dorsolateral grey-white matter transition zone and lateral fascicle (red arrows) next to an occluded arterial blood vessel with a pink fibrocartilaginous embolus (yellow arrow). PAS stain. (Photo courtesy Kaspar Matiasek)

Cerebrospinal fluid analysis

CSF analysis may be normal or may reveal non-specific abnormalities including xanthochromia, elevated protein concentration and mild pleocytosis. PCR for different infectious agents in CSF may help to rule out specific aetiologies of meningomyelitis (e.g. canine distemper virus, *Toxoplasma gondii* and *Neospora caninum*).

Myelography

The main value of myelography in the diagnosis of ischaemic myelopathy is the exclusion of other causes of peracute/acute myelopathy and in particular of those resulting in spinal cord compression (e.g. intervertebral disc extrusion, epidural haemorrhage). In dogs and cats with ischaemic myelopathy, the myelogram may be normal or may reveal an intramedullary pattern suggestive of spinal cord swelling in the acute stage of the disease. However, this latter finding may also be observed with other causes of myelopathy including acute non-compressive nucleus pulposus extrusion. The width of the underlying intervertebral disc spaces has to be assessed carefully on good quality radiographs with optimal patient positioning. The presence of a collapsed intervertebral disc space beneath the area of spinal cord swelling should raise the suspicion of acute non-compressive nucleus pulposus extrusion.

Computed tomography

CT can also help to rule out other causes of acute myelopathy. An intramedullary pattern of spinal cord swelling may be seen on a CT myelogram in the acute stage of ischaemic myelopathy.

Histology

A definitive diagnosis of ischaemic myelopathy can be reached only by histological examination of the affected spinal cord segment(s). Histological examination reveals necrosis within the affected spinal cord segment(s) (**268**). Commonly, grey and white matter are both involved, with the former being more severely affected than the latter. The distribution of the lesion reflects the territory of the embolized vessel(s) and, therefore, is frequently asymmetric. The margins of the lesion tend to be well delineated from normal tissue.

Lesion evolution occurs in three stages: (1) ischaemic necrosis; (2) resorption; and (3) cavitation and gliosis. The type and spatial distribution of the lesion are diagnostic for an ischaemic myelopathy. However, proof of an embolic aetiology relies on the histological evidence of cellular or acellular material in one or more spinal cord vessel(s) (arteries, arterioles and/or veins) within or near

the lesion or, occasionally, in nerve root vasculature. In the majority of cases reported in the literature, the embolized material had histological and histochemical staining characteristic of fibrocartilage that is most probably derived from the nucleus pulposus. Infarcted areas are usually initially ischaemic, but sometimes may be accompanied by haemorrhage.

TREATMENT

Treatment of ischaemic myelopathy includes reducing secondary spinal cord injury (maintenance of spinal cord perfusion, neuroprotection), nursing care and physiotherapy.

Maintenance of spinal cord perfusion usually does not require any intervention in patients with ischaemic myelopathy as systemic BP, ventilation and oxygenation are usually normal. However, in patients with concurrent cardiovascular or respiratory disease or with neurological impairment of ventilation (e.g. severe cervical spinal cord lesions affecting phrenic nerve function) it is important to monitor and maintain systemic BP, ventilation and oxygenation within normal limits.

Neuroprotective agents, such as methylprednisolone sodium succinate and polyethylene glycol, could help to minimize the secondary injury phenomenon triggered by the ischaemic insult. However, the clinical benefits of these drugs require further investigation and there are increasing concerns about the adverse effects of methylprednisolone sodium succinate. These and other neuroprotective agents are described in detail in Chapter 21 (Spinal trauma).

To date, there is no evidence that administration of either methylprednisolone sodium succinate, other types of glucocorticoids or NSAIDs improves outcome in dogs with ischaemic myelopathy. However, no prospective randomized controlled clinical trial has been performed to investigate the value of these or other drugs in patients with ischaemic myelopathy.

Excellent nursing care and physiotherapy play an essential role in the management of neurological patients and particularly of those that are recumbent and severely impaired. Nursing care includes bladder and bowel management, adequate bedding, regular turning, skin care to prevent decubital ulcers and urine scalding, care of the respiratory system (prevention/treatment of hypoventilation, aspiration pneumonia, pulmonary atelectasis) and adequate nutrition. Physiotherapy stimulates neuronal plasticity and therefore maximizes functional recovery mediated by spared neural tissue. In addition, physiotherapy plays an important role in limiting and reversing disuse and immobilization changes such as muscle atrophy and muscle and joint contractures. Nursing care and physiotherapy are described in detail in Chapter 32 (Postoperative supportive care and physical rehabilitation).

PROGNOSIS

The prognosis depends on the severity of the ischaemic insult and the extent of the ischaemic injury. The latter can be assessed clinically (severity of neurological dysfunction) and by means of MRI (longitudinal and transverse extent of the lesion).

In the author's MRI-based study, severity of neurological signs at the time of initial examination was significantly associated with the extent of the lesion on MRI and with outcome. The extent of the lesion on MRI was defined as the ratio between the length of the intramedullary hyperintensity on mid-sagittal T2-weighted images and the length of the vertebral body (referred to as the lesion length:vertebral length ratio) of C6 (in dogs with cervical lesions) or L2 (in dogs with thoracolumbar lesions), and as the cross-sectional area of the largest intramedullary hyperintensity on transverse T2-weighted images expressed as a percentage of the cross-sectional area of the spinal cord at the same level (referred to as percentage cross-sectional area of the lesion). The lesion length:vertebral length ratio and the percentage cross-sectional area of the lesion were both significantly associated with outcome. The sensitivity of using a lesion length:vertebral length ratio >2.0 or a percentage cross-sectional area of the lesion ≥67% to predict an unsuccessful outcome was 100%.

Other negative prognostic factors reported in previous studies on canine ischaemic myelopathy include the presence of LMN signs, symmetrical neurological deficits and loss of nociception. The latter is the most consistent and significant negative prognostic factor in different clinical studies on ischaemic myelopathy as well as traumatic spinal cord injury. Another factor that influences the prognosis in dogs with ischaemic myelopathy is the owner's commitment to pursue nursing care and physiotherapy, which can be quite extensive and intense, especially in large breed dogs.

Two studies have suggested that the presence of CSF abnormalities (increased protein concentration +/- pleocytosis) may be associated with a poorer outcome in dogs with ischaemic myelopathy. However, in the author's MRI-based study there was no association between the presence of CSF abnormalities and outcome or the extent of the intramedullary lesion on MRI.

Success rates vary among studies, probably depending on differences in inclusion criteria, severity and distribution of ischaemic lesions, definition of outcome and owner's commitment. The two most recent studies on a large number of dogs with ischaemic myelopathy have reported a favourable outcome in 42/50 (84%) dogs and 49/75 (65%) dogs, respectively.

Most dogs and cats show an improvement within the first 2 weeks of onset of neurological signs. This rapid improvement is most probably due to the resolution of oedema surrounding the infarcted area of the spinal cord. In the author's MRI-based study, mean time intervals between onset of neurological signs and recovery of voluntary motor activity, unassisted ambulation and maximal recovery were 6 days (range, 2.5–15 days), 11 days (range, 4–136 days) and 3.75 months (range, 1–12 months), respectively. In another study the mean time to recovery of unassisted ambulation was 12 ± 9.77 days in 49 dogs. To date no statistically significant association has been identified between recovery times and neuroanatomical localization, severity of motor dysfunction, involvement of an intumescence and site or extent of the lesion on MRI.

Even though reported cases are limited, it is likely that the prognosis for cats receiving adequate nursing care is as good as for dogs.

INFECTIOUS AND INFLAMMATORY DISEASES OF THE CNS

Scott Schatzberg & Peter Nghiem

INTRODUCTION

Animals with meningoencephalomyelitis (MEM) typically are presented for acutely progressive, focal to multifocal neurological signs. Patients should be stabilized initially if systemic derangements (cardiovascular or respiratory) or evidence of increased ICP are/is present. When the patient is stable, the clinician should attempt to differentiate between infectious and idiopathic MEM based on the signalment, physical examination findings, the presence/absence of systemic signs, and infectious disease testing. Differentiation between infectious and idiopathic MEM is critical, and may require CSF analysis and advanced neuroimaging. Once an infectious or idiopathic differential diagnosis list is generated, the most appropriate diagnostic plan can be implemented.

MENINGOENCEPHALOMYELITIS

Overview

MEM is defined as inflammation of the meninges (dura, arachnoid and pia mater) and the neuroparenchyma (e.g. forebrain, brainstem, cerebellum and/or spinal cord). Clinical signs of encephalitis reflect the location of the lesion(s) (forebrain, brainstem or cerebellum). Clinical signs of myelitis reflect whether the spinal cord lesion(s) are within the UMN or LMN system, or both. Pain and/or hyperaesthesia is/are most common with meningitis (brain or spinal cord).

Due to the typical acute and progressive nature of MEM, animals are commonly presented for emergency evaluation. Based on the neuroanatomical localization, it is imperative to formulate an accurate differential diagnosis in order to institute the correct diagnostic recommendations and therapies.

Aetiology/pathophysiology

MEM may be caused by an infectious agent or associated with an idiopathic inflammatory condition of the CNS. Canine and feline MEM have been reported throughout the world. However, infectious MEMs are more prevalent in certain geographical locations (*Table* 77).

Table 77 Global prevalence of infectious MEM*

REGION	INFECTIOUS AGENTS
North America	*A. platys, Aspergillus* spp., *Babesia* spp., *B. dermatitidis*, CDV, *C. immitis*, *C. neoformans*, *E. canis*, FIPV, *H. capsulatum*, *N. caninum*, rabies virus, *R. rickettsii*, *T. gondii*
Central America	*B. dermatitidis*, CDV, *C. immitis*, FIPV, *N. caninum*, rabies virus, *T. gondii*
South America	CDV, *C. immitis*, *C. neoformans*, FIPV, *H. capsulatum*, *N. caninum*, rabies virus, *R. rickettsii*, *T. gondii*
Europe	*Aspergillus* spp., *B. dermatitidis*, CDV, *C. neoformans*, *E. canis*, FIPV, *N. caninum*, rabies virus, *R. rickettsii*, *T. gondii*
Northern Asia	CDV, *C. neoformans*, *E. canis*, FIPV, rabies virus, *T. gondii*
Southeast Asia	*B. dermatitidis*, CDV, *C. neoformans*, *E. canis*, FIPV, rabies virus, *T. gondii*
Africa	*B. dermatitidis*, CDV, *C. neoformans*, *E. canis*, FIPV, rabies virus, *T. gondii*
Australia	*A. platys, Aspergillus* spp., CDV, *C. neoformans*, *E. canis*, FIPV, rabies virus, *T. gondii*

*Risk of exposure to the most common diseases in these areas. Great Britain, Scandinavia, New Zealand, Japan and much of Australia are considered rabies 'free'.

Table 78 **Infectious agents known to cause acute meningoencephalomyelitis**

AGENT	DOGS	CATS
Bacterial	Aerobic Anaerobic	Aerobic Anaerobic
Rickettsial	*Rickettsia rickettsii* *Ehrlichia* spp. *Anaplasma* spp.	
Viral	Canine distemper virus (CDV) Rabies virus West Nile virus (North America) Tick-borne encephalitis virus (Europe and Asia) Borna disease virus (Europe and Japan) Eastern equine encephalitis virus (North America; rare)	Feline infectious peritonitis virus (FIPV) Feline leukaemia virus (FeLV) Borna disease virus (Europe and Japan)
Protozoal	*Neospora caninum* *Toxoplasma gondii* *Sarcocystis canis* (rare) *Encephalitozoon cuniculi* (rare) *Trypanosoma cruzi* (rare) *Acanthomoeba* spp. (rare) *Babesia* spp. (rare) *Leishmania* spp. (Mediterranean basin and Portugal)	*Toxoplasma gondii* *Babesia* spp. *Leishmania* spp. (Mediterranean basin and Portugal)
Fungal	*Cryptococcus* spp. *Coccidioides immitis* *Blastomyces dermatitidis* *Histoplasma capsulatum* (rare) *Aspergillus* spp. (rare)	*Cryptococcus* spp. *Coccidioides immitis* *Blastomyces dermatitidis* *Histoplasma capsulatum* (rare) *Aspergillus* spp. (rare)
Parasitic	Cuterebra larva migration (rare) *Dirofilaria immitis* – abberant migration (rare)	Cuterebra larva migration (rare) *Dirofilaria immitis* – abberant migration (rare)

Infectious meningoencephalomyelitis

Infectious agents are confirmed uncommonly in cases of MEM, but are important differentials nonetheless. Pathogens that may cause canine or feline MEM include bacteria, viruses, protozoa, fungi, and parasites. MEM most commonly occurs in young or immunocompromised animals; however, any dog or cat may develop a CNS infection. Some infectious agents are capable of affecting multiple organ systems in addition to the CNS, which may prove helpful in distinguishing CNS infections from an idiopathic meningoencephalitis (ME). The severity of infection is dependent on several factors including: the status of the animal's immune system at the time of inoculation; strength of the animal's immune response during active infection; nutritional status of the animal; strain and virulence factors of the infectious agent; and environmental factors. Clearance of the infectious agents is dependent on these factors as well; however, some pathogens may enter a dormant stage within the host without producing clinical disease. Recrudescence of such organisms may occur with or without clinically apparent disease.

Infectious agents known to cause acute MEM in the dog and cat are listed in *Table 78*.

Bacterial and rickettsial meningoencephalomyelitis

Bacterial meningitis and CNS abscesses are among the most important differentials for MEM that may lead to an emergency presentation. Bacterial meningitis may result from several different mechanisms including: haematogenous spread from other foci within the body; direct inoculation from traumatic wounds or needles following CSF acquisition; or direct extension from other structures of the head (eyes, ears, cribriform plate). Bacteria that have been reported in association with meningitis include *Staphylococcus* spp., *Pasteurella* spp., *Escherichia coli*, *Actinomyces* spp., *Nocardia* spp., *Klebsiella* spp., *Peptostreptococcus* spp., *Eubacterium* spp. and *Bacteroides* spp. Pathological findings include infiltration of mononuclear and polymorphonuclear (PMN) cells into the leptomeninges. If the underlying neuroparenchyma is affected, necrosis of the grey and white matter may occur due to direct neuronal injury or thrombosis.

CNS abscesses and empyema, similar to bacterial meningitis, may result from haematogenous spread from other foci within the body, direct inoculation or direct extension from other structures of the head (nasal cavity and sinuses, eye, ear). Immature and immunocompromised animals are at a greater risk for the development of CNS abscesses. Similar organisms to those responsible for bacterial meningitis have been reported including *Staphylococcus* spp., *Streptococcus* spp., *Nocardia* spp., *Pasteurella* spp., *Actinomyces* spp., *Fusobacterium* spp., *Bacteroides* spp. and *Peptostreptococcus* spp. Occasionally, fungal organisms may produce CNS abscesses. The progression of abscess formation includes inflammation of the associated anatomical structure (i.e. encephalitis, myelitis) followed by capsular formation. Oedema and significant mass effect are often features of this disease in the brain (**269**). Additional pathological findings include rings of organisms with infiltration of mononuclear and PMN cells, diffuse leptomeningitis, reactive astrocytes, gliosis and cerebral oedema outside the capsule.

Rickettsial organisms, including *Rickettsia rickettsii* and *Ehrlichia canis*, are transmitted to dogs via tick vectors. Once rickettsiae infect a dog or cat, they enter endothelial cells, leading to a vasculitis of multiple organ systems including the CNS. Lymphoplasmacytic meningitis predominates; however, MEM occurs occasionally when the underlying neuroparenchyma (forebrain, brainstem and cerebellum) is affected.



▲ **269** **Transverse T1-weighted post-contrast (a) and T2-weighted (b) images of the brain of a cat with subdural empyema (arrows) causing severe mass effect with marked displacement of the falx cerebri. (Photo courtesy Laurent Garosi)**

Viral meningoencephalomyelitis

Recently, there have been sporadic reports of flavivirus (tick-borne encephalitis virus, west Nile virus), bornavirus and Eastern equine encephalitis infection in dogs, suggesting that canine viral ME is more prevalent than currently accepted. However, the aetiologies for the majority of cases of canine ME remain elusive, potentially because of current limitations for pathogen detection in routine diagnostic testing. The most common viral causes of acute MEM appear to be rabies and canine distemper virus (CDV).

Rabies infections have been reported more frequently in cats than in dogs in the US, with infection being uniformly fatal in both species. Rabies virus is considered endemic in most of the world except Great Britain, Scandinavia, New Zealand, Japan and much of Australia. After the virus is introduced through a bite of an infected animal, it then replicates and travels within peripheral nerves to the brain, resulting in a non-suppurative polioencephalomyelitis and craniospinal ganglionitis. The incubation period is 2 weeks to 6 months. Areas of the CNS affected are widespread and commonly include the brainstem and cerebral hemispheres. Occasionally, dogs and cats can develop post-vaccinal rabies if the vaccine is given during times of stress (e.g. boarding, surgery, systemic illness).

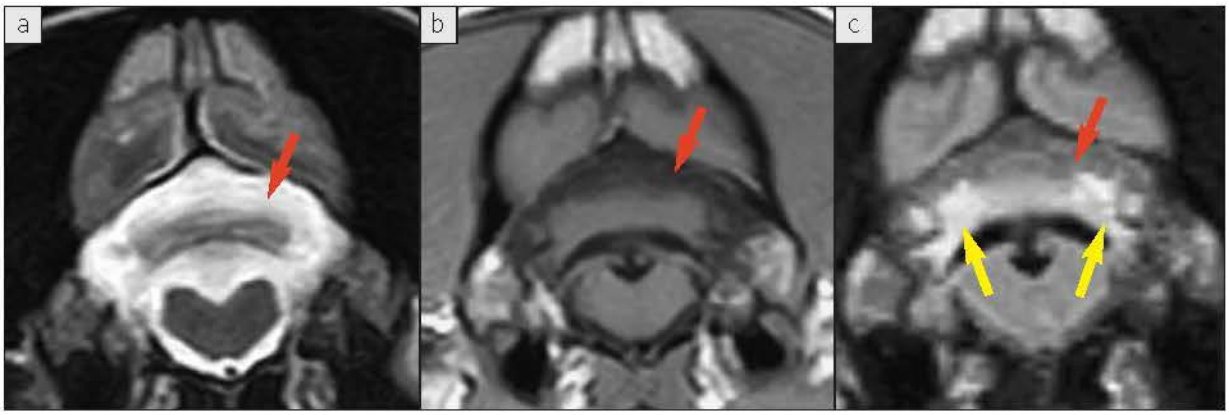
CDV, in contrast to rabies, is not uniformly fatal. Three forms of CDV occur in dogs, with encephalomyelitis in immature dogs (3–6 months of age most frequently) presenting most commonly as an acute neurological emergency. The other forms occur in adult to geriatric dogs, which are rarely presented for acute neurological signs. Dogs are inoculated with the virus via exposure to infected respiratory droplets. An infected dog with CDV can transmit the virus up to 60–90 days post infection. The virus spreads haematogenously to other organ systems including skin, endocrine and exocrine glands, epithelium of the gastrointestinal, respiratory and genitourinary tracts, and the CNS. Direct viral replication results in neuronal injury and necrosis, with multifocal lesions in grey and white matter. In the subacute stages, white matter tends to be more affected than grey matter. CNS lesions generally consist of varying degrees of lymphoplasmacytic inflammation, demyelination and necrosis. Post-vaccinal canine distemper encephalitis typically occurs in dogs <6 months of age and is associated with administration of a live virus. The pathogenesis is speculative, but may involve immunosuppression of the dog, latent CDV infection, inadequate attenuation of the vaccine or other vaccine component interactions.

FIP virus is the causative agent of CNS FIP, a syndrome that is uniformly fatal in cats. FIP virus is a mutated strain of the non-pathogenic feline enteric coronavirus. FIP occurs in two clinical forms: the effusive (wet) form and the non-effusive (dry) form. The more common effusive form causes systemic disease secondary to an exuberant humoral immune response, characterized by a fibrinous peritonitis and pleuritis. The non-effusive form results from a combined humoral immune and partial cell-mediated immune response. This 'eye and brain' form affects the meninges, CNS neuroparenchyma and uvea. Pathological findings within the CNS include perivascular pyogranulomatous infiltration of the leptomeninges, neuroparenchyma of the brain and spinal cord, choroid plexus and ependyma. Other common findings include subependymal necrosis, ventricular dilatation, hydrocephalus, panophthalmitis and vascular degeneration.

Protozoal meningoencephalomyelitis

Protozoal organisms are important causes of MEM in dogs and cats. Dogs and cats are the definitive hosts for *Neospora caninum* and *Toxoplasma gondii*, respectively. Transmission of *T. gondii* occurs by carnivorous ingestion (most common), orofaecal contamination or transplacentally. Multiple organ involvement, including ocular, pulmonary, liver and CNS, is often present concurrently. A mixed cell infiltrate predominated by lymphocytes is typically present. Clinical toxoplasmosis most commonly affects dogs <1 year of age and immunocompromised geriatric dogs. Toxoplasmosis may be associated with CDV or other infections, such as ehrlichiosis, or with glucocorticoid therapy. Neurological signs associated with *T. gondii* infection include MEM and/or myositis–polyradiculoneuritis.

The life cycle of *N. caninum* is not completely understood, but infection during the neonatal period is suspected. In addition to encephalomyelitis, multiple organ system involvement may also occur with *N. caninum* infection. In juvenile dogs <6 months of age, myositis, ascending polyradiculoneuritis and encephalomyelitis predominate. Rigid limb contracture and arthrogryposis may occur as a result of the myositis. Severe MEM tends to be rare with *N. caninum* infection in young dogs. In dogs >1 year of age, MEM (commonly cerebellitis) is the more typical presentation (**270**).



▲ 270 Transverse T2-weighted (a), T1-weighted (b) and T2-weighted FLAIR (c) images of the caudal fossa of a 9-year-old West Highland White Terrier with *Neospora* infection. The diffusely atrophied cerebellum is surrounded by a thick T2-weighted hyperintense and T1-weighted hypointense signal that does not suppress on FLAIR sequences (red arrow). Additionally, there are bilaterally symmetrical FLAIR hyperintensities within the cerebellar white matter (yellow arrows). (Photo courtesy Laurent Garosi)

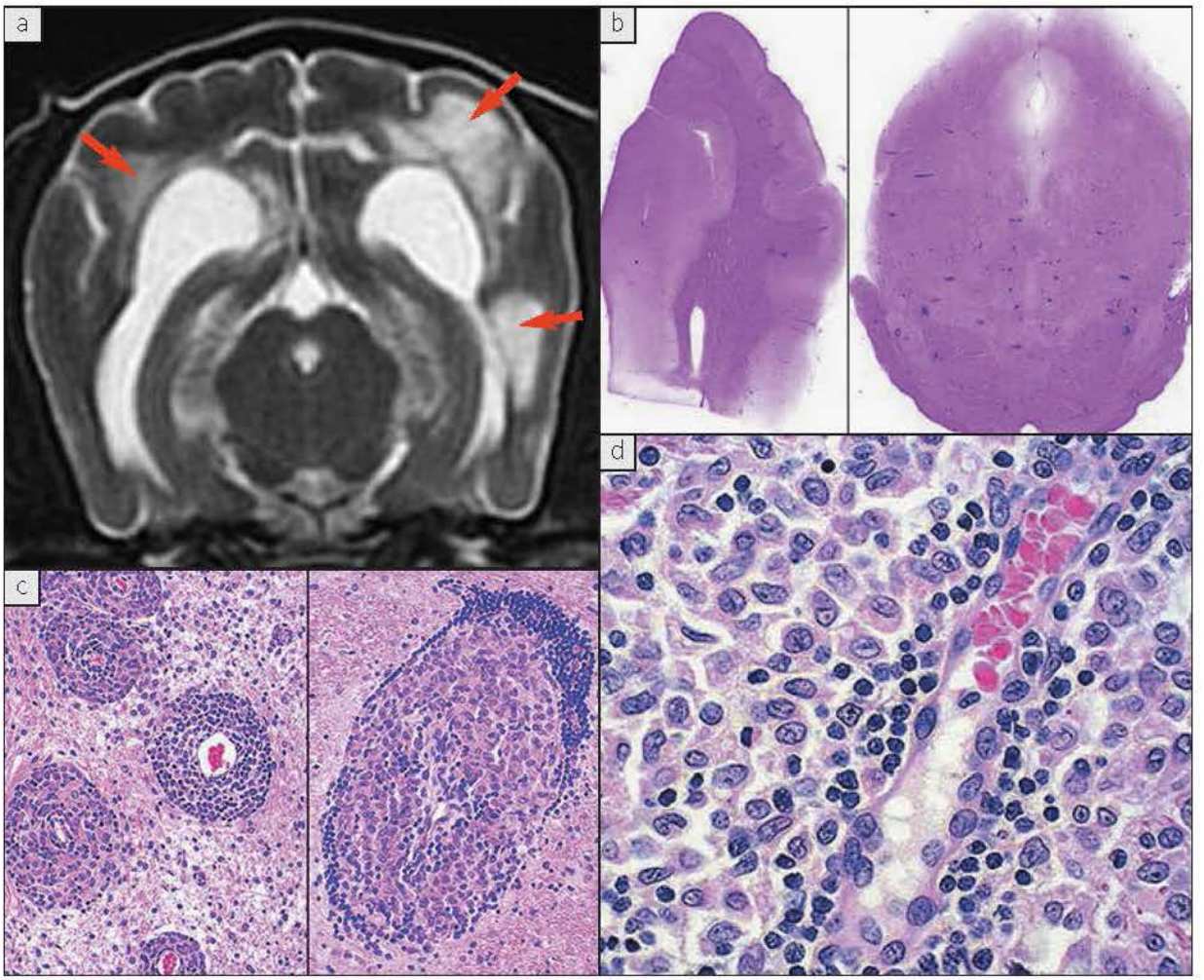
Fungal and parasitic meningoencephalomyelitis

Mycotic agents sporadically cause MEM in dogs and cats. *Cryptococcus neoformans* is the most common CNS fungal infection in cats and dogs. *Blastomyces dermatitidis*, *Coccidioides immitis*, *Histoplasma capsulatum* and *Aspergillus* spp. have also been reported to cause CNS infection in dogs. The most common route of inoculation for fungal organisms is inhalation. Morphological conversion to the yeast form occurs in the animal and haematogenous or lymphatic spread to other organ systems, including the respiratory, skeletal, integument, ocular and musculoskeletal systems, may occur. Fungal organisms may cause an acute, focal or multifocal-diffuse MEM with a mixed cell parenchymal infiltrate (granulomatous or pyogranulomatous). Aberrant migration of parasitic larvae to the CNS, including *Cuterebra* spp. (common in cats) and *Dirofilaria immitis*, may also produce MEM in dogs and cats.

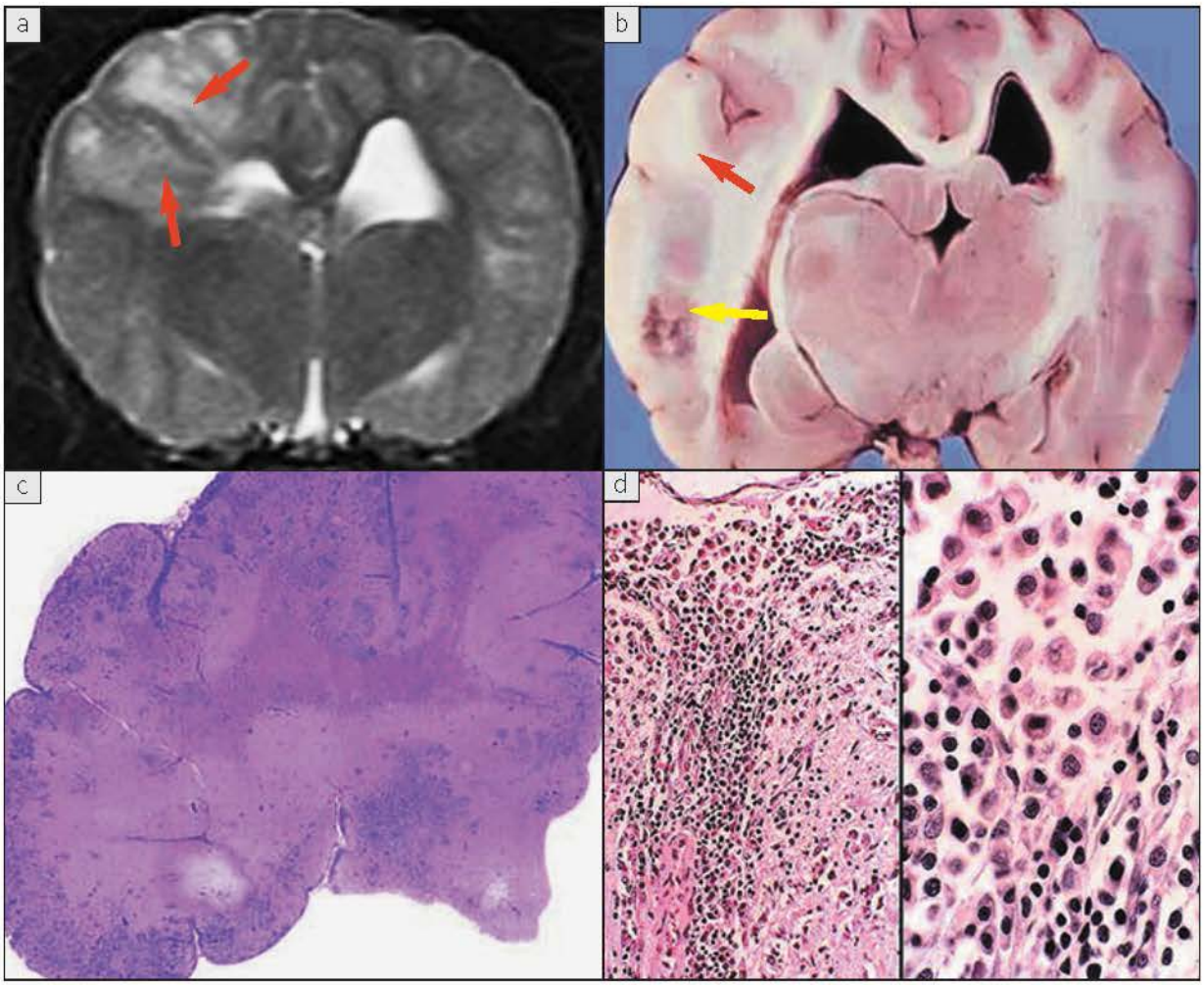
Idiopathic meningoencephalomyelitis

Idiopathic MEM occurs commonly in the dog, but seems to be extremely rare in the cat. GME, NME, NLE, SRMA and idiopathic tremor syndrome comprise the most common inflammatory conditions of the canine CNS. While each disease has unique histopathological features, these canine MEMs collectively seem to be aberrant immune responses directed against the CNS.

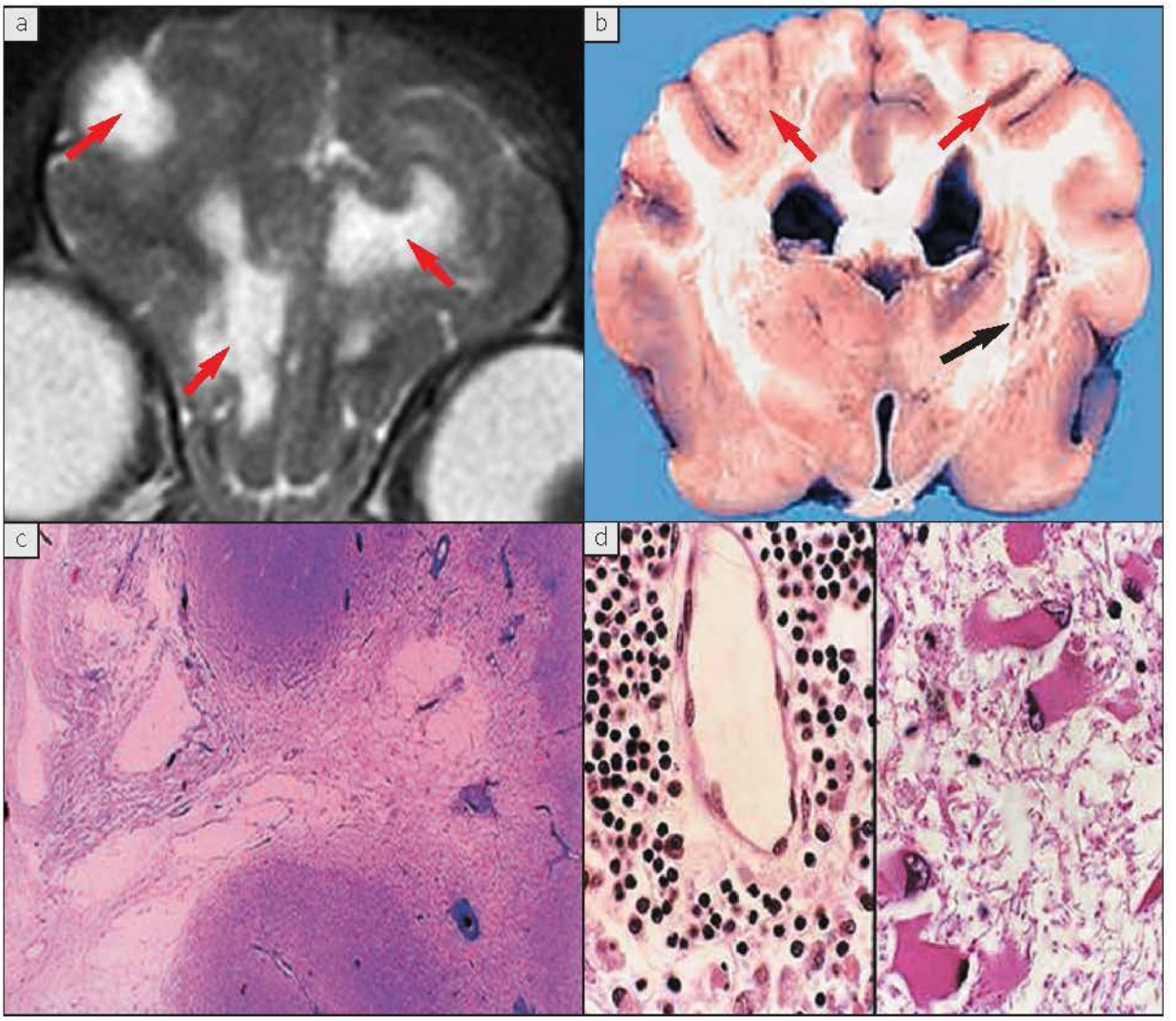
The aetiopathogenesis of GME, NME and NLE is probably multifactorial: familial predisposition, infectious agents and immunopathologic mechanisms all may play a role in disease pathogenesis. GME is responsible for up to 25% of canine CNS disease. Three morphological forms of GME have been described: disseminated, focal and ocular. Typical histopathological lesions include concentric proliferation of inflammatory cells around blood vessels, predominantly of the white matter of the CNS (**271**, next page). Clinical signs reflect the location of the lesions, and GME typically is fatal if not treated aggressively with immunosuppression.



▲ 271 Disseminated granulomatous meningoencephalitis. (a) Transverse T2-weighted MR image at the level of the midbrain and cerebral hemispheres. Multiple, infiltrative hyperintensities (arrows) are scattered throughout the central white matter. These hyperintense lesions probably represent a combination of oedema and inflammation. (b) Subgross GME lesions seen here in the cerebrum and midbrain. (c) The cells in the perivascular cuffs include lymphocytes, plasma cells and large, pale histiocytic cells. The left panel shows coalescing cuffs. When several cuffs coalesce, a grossly visible lesion will be evident. Despite the density of the cuffs, there is little tendency for cells to infiltrate the parenchyma. (d) High-magnification view of lymphocytes and large histiocytoid cells in a perivascular cuff. Plasma cells, rare in this image, may also be present. (From Talarico LR, Schatzberg SJ (2010) Idiopathic granulomatous and necrotizing inflammatory disorders of the canine central nervous system: a review and future perspectives. *J Small Anim Pract* 51:138–149, with permission.)



▲ 272 Necrotizing meningoencephalitis. (a) Transverse T2-weighted MR image at the level of the thalamus and cerebral hemispheres. Note the asymmetric, hyperintense, infiltrative lesions affecting the prosencephalon (arrows). The demarcation between grey and white matter is obscured and no evidence of cavitation is seen. (b) Transverse section of the brain at the level of the diencephalon. Inflammation dulls the white matter and characteristically effaces the junction of grey and white matter in the cerebrum (red arrow). Note also the asymmetric swelling, midline shift, slight ventricular enlargement and focal cavitation (yellow arrow). (c) Occipital lobe of a Pomeranian dog. A diffuse infiltrative lesion is present extending from the cortical surface through the grey matter and multifocally entering the white matter. This was a substantially unilateral disease. (d) Cerebral cortex. Meningeal mixed inflammatory infiltrates, which include large and small mononuclear cells and plasma cells. (From Talarico LR, Schatzberg SJ (2010) Idiopathic granulomatous and necrotizing inflammatory disorders of the canine central nervous system: a review and future perspectives. *J Small Anim Pract* 51:138–149, with permission.)



▲ 273 Necrotizing leucoencephalitis. (a) Transverse T2-weighted MR image at the level of the frontoparietal lobes. Multiple, asymmetric bilateral forebrain lesions, mainly affecting the subcortical white matter, are present (arrows). (b) Asymmetric, cavitating lesions in the corona radiata (red arrows), internal capsule (black arrow) and thalamocortical fibres. (c) Low-magnification view. Corona radiata with intense oedema, dissolution of white matter, early cavitations and residual perivascular cuffing. (d) Corona radiata, high magnification. Left panel: lymphoid and histiocytoid cells cuffing a vessel. Right panel: large reactive astrocytes (gemistocytes). (From Talarico LR, Schatzberg SJ (2010) Idiopathic granulomatous and necrotizing inflammatory disorders of the canine central nervous system: a review and future perspectives. *J Small Anim Pract* 51:138–149, with permission.)

NME and NLE are CNS inflammatory disorders with similarly elusive aetiopathogeneses to that of GME. Historically referred to as 'Pug Dog encephalitis' and 'necrotizing encephalitis of Yorkshire Terriers', respectively, these idiopathic MEs have now been reported in many other toy breed dogs. Although notable differences in lesion topography exist between them, the hallmarks of both diseases include non-suppurative ME and variable degrees of cerebral necrosis (**272** page 347, **273**). Clinical signs typically are progressive, reflect the location of cerebral lesions and include seizures, lethargy, circling, visual deficits and ultimately death.

Recently, the authors evaluated pedigree information on a large cohort of Pugs and demonstrated a strong familial inheritance pattern for NME. While this transmission pattern is not surprising, a simple Mendelian inheritance pattern could not be demonstrated. The latter suggests that NME is a multifactorial disorder. Previous screens for viral aetiologies revealed negative results. Molecular studies are ongoing to assess for genetic susceptibility loci and a diverse group of potential infectious triggers that may lead to immune dysregulation in GME, NME and NLE.

SRMA is a systemic immune disorder characterized by inflammatory, stenosing lesions of the meninges and the associated arteries. The characteristic lesion associated with SRMA is a necrotizing fibrinoid arteritis consisting predominantly of neutrophils and scattered lymphocytes, plasma cells and macrophages. Vasculitis is more common in the leptomeninges of the spinal cord than around the brain, and lesions are occasionally present in the thyroid, heart and mediastinum. Extensive leptomeningeal haemorrhages and meningeal plaques may be apparent grossly. Acute thrombosis of the vasculature may create ischaemic changes.

Idiopathic tremor syndrome is a mild, diffuse, non-suppurative encephalomyelitis, with perivascular cuffing by lymphoplasmacytic mononuclear cells. The lesions affect the CNS diffusely, including the ascending sensory tracts, descending motor tracts and, occasionally, the cerebral and cerebellar hemispheres. CNS myelin is unaffected. The exact aetiopathogenesis is unknown, but an autoimmune disorder affecting neurotransmitter synthesis has been considered. Other potential triggers include pathogens or endogenous epitopes associated with neurotransmitters or cell membrane receptors.

SIGNALMENT AND HISTORY

Infectious meningoencephalomyelitis

Signalment and history may aid in prioritizing infectious MEM over idiopathic MEM. For example, an inappropriate vaccination history may raise the index of suspicion for CDV or rabies MEM. Similarly, a history of travel to endemic areas or recent tick exposure may suggest fungal or rickettsial disease, respectively. The most common age group in which FIP occurs in cats is between 6 months and 2 years of age, followed by geriatric cats >14 years of age. There are no breed predispositions for FIP; however, intact male cats and those in stressful environments (e.g. catteries) may be at an increased risk.

Idiopathic meningoencephalomyelitis

Breed and age are particularly important for the recognition of the idiopathic MEMs. GME is most common in females and toy and terrier breeds, but both sexes and all breeds may be affected. For GME, the mean age of onset of neurological signs is 5–6 years (range: 6 months to 12 years). NME and NLE have been reported in various toy breeds including the Pug, Maltese, Chihuahua, Yorkshire Terrier, Pekingese, West Highland White Terrier, Boston Terrier, Japanese Spitz and Miniature Pinscher. The age of onset of neurological signs associated with NME varies from 6 months to 7 years of age and most commonly occurs in young dogs, with a mean age of 29 months. NLE typically manifests between 4 months and 10 year of age, with a mean age of onset of 4.5 years.

SRMA may occur in any breed of dog, although young Beagles, Boxers, Bernese Mountain Dogs, German Short-haired Pointers and Nova Scotia Duck Tolling Retrievers are overrepresented. The age of onset of neurological signs associated with SRMA is commonly between 6 and 18 months, with a range from 4 months to 7 years.

Idiopathic tremor syndrome affects predominately small breed dogs, most commonly Maltese, Cocker Spaniels and West Highland White Terriers. Affected dogs typically present between 1 and 5 years of age, may be any colour (although often are white) and typically weigh <15 kg.

CLINICAL PRESENTATION

General meningoencephalomyelitis

The clinical presentation of infectious or idiopathic MEM is variable, as any part of the neuraxis may be affected by inflammation. MEM may be focal, multifocal or diffuse in nature and patients often present with symmetric neurological signs (**274**). As mentioned previously, clinical signs of encephalomyelitis reflect the location of the lesion(s). Animals with meningitis may be presented for discomfort in the acute stage of disease, but may progress to manifest obvious neurological deficits in the later stages (if the underlying neuroparenchyma becomes inflamed).

Infectious meningoencephalomyelitis

Neurological signs caused by infectious agents are extremely variable and are dependent on the neuroanatomical location of the lesion(s). Although the neurological signs alone should not form the basis of a diagnosis of infectious MEM, some infectious agents cause 'classic' neurological signs. For example, CDV often produces generalized flexor spasms of the muscles of the limbs, neck and/or masticatory muscles, so-called CDV myoclonus. Rabies infection may cause 'paralytic (dumb)' or 'furious' variants of disease, caused by ascending LMN paresis and limbic system involvement, respectively. Toxoplasmosis and neosporosis often affect puppies with a combination of LMN signs and MEM. Cats with CNS FIP typically are presented for acutely progressive, multifocal to diffuse neurological signs including seizures, behavioural abnormalities, cerebellovestibular signs, GP ataxia and various degrees of fore- and hindlimb paresis to paralysis.

The typical presentation for bacterial meningitis and/or CNS abscesses is an acutely progressive condition with variable neurological deficits. Clinical signs of meningitis include cervical hyperaesthesia, low head carriage and pain on palpation. In addition, vomiting, bradycardia and seizures may occur. CNS abscesses often lead to a focal localization; however, a multifocal localization may be present with multiple abscesses. If an infectious MEM is suspected, systemic signs should be evaluated carefully. Infectious CNS diseases are associated with systemic signs more frequently than the idiopathic MEMs, including:

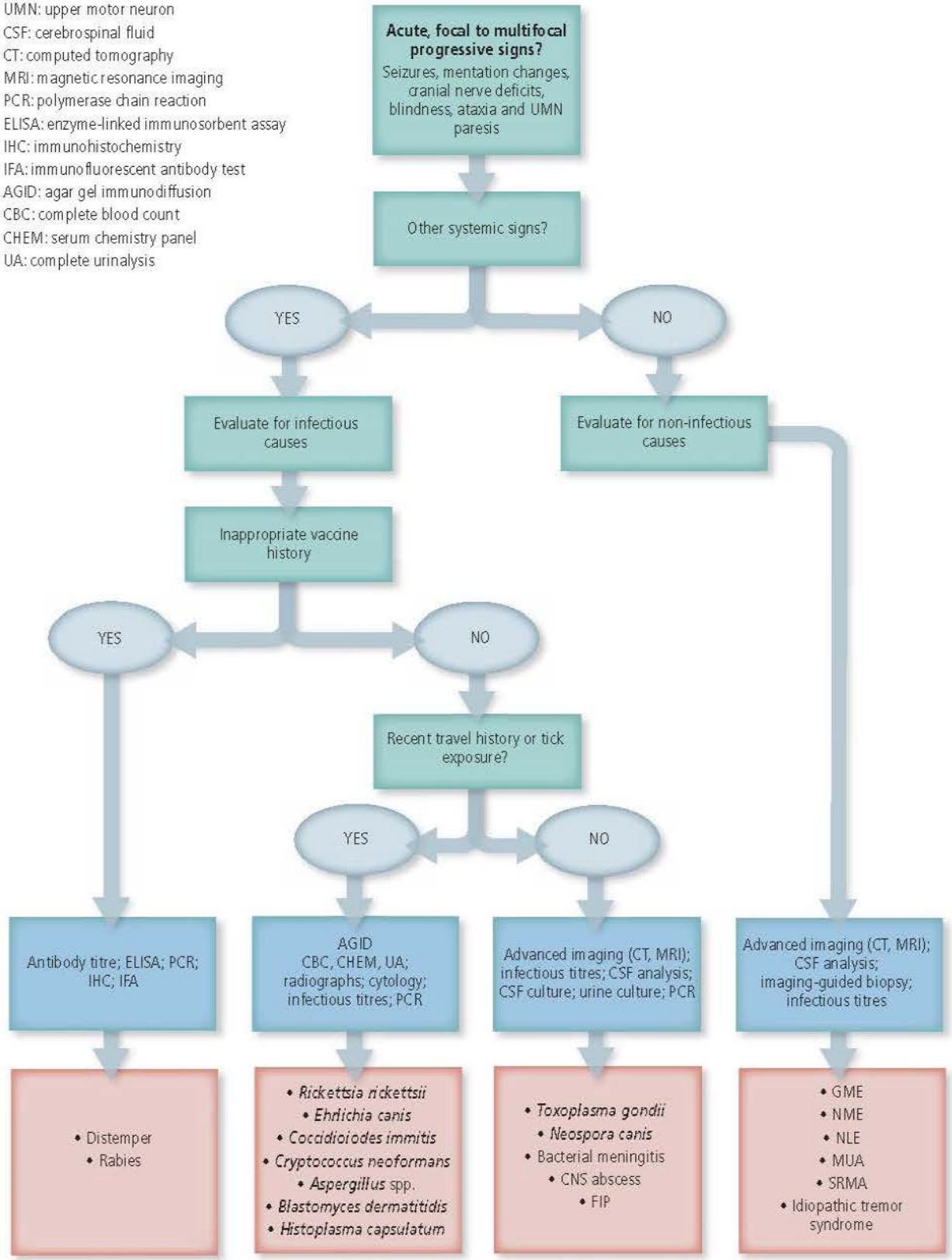
- A source or foci (e.g. liver abscess, pneumonia, bacterial endocarditis) or evidence of direct extension from the eyes, ears or nasal cavity with bacterial MEM and bacterial abscesses.
- Pulmonary, gastrointestinal, ocular and integumentary abnormalities with CDV infection.
- Focal haemorrhages (secondary to vasculitis), fundic abnormalities (haemorrhage, exudate), fever, peripheral oedema, thrombocytopenia, lymphadenopathy, renal disease and arthropathy with rickettsial infections.
- Multisystem involvement, including pulmonary, skin, musculoskeletal, ocular, and internal organ involvement, with fungal and protozoal disease.
- Fever, hyperglobulinaemia and chorioretinitis with FIP.

Idiopathic meningoencephalomyelitis

As with the infectious MEMs, the neurological signs of the idiopathic disorders tend to be reflective of the neuroanatomical locations of the lesion(s). Disseminated GME often presents as an acutely progressive, multifocal neurological disease that may be fatal if left untreated. Neurological deficits referable to the caudal cranial fossa (vestibulocerebellar signs) and cervical spinal cord, in addition to seizures and visual deficits, have been reported most frequently. Neurological signs associated with the uncommon, focal form of GME may be acute or slowly progressive and they are suggestive of a single space-occupying mass lesion. Forebrain signs were reported most frequently with focal GME in one study, although the brainstem or spinal cord may be affected. The ocular form of GME manifests with an acute onset of visual impairment, variable pupillary changes (commonly dilated and unresponsive), variable degrees of optic nerve oedema and occasionally chorioretinitis, especially in the non-tapetal fundus. Dogs with ocular GME may concurrently have, or progress to develop, disseminated CNS lesions.

▶ **274 Algorithm for diagnosis of acute meningoencephalomyelitis.**

UMN: upper motor neuron
CSF: cerebrospinal fluid
CT: computed tomography
MRI: magnetic resonance imaging
PCR: polymerase chain reaction
ELISA: enzyme-linked immunosorbent assay
IHC: immunohistochemistry
IFA: immunofluorescent antibody test
AGID: agar gel immunodiffusion
CBC: complete blood count
CHEM: serum chemistry panel
UA: complete urinalysis



Dogs with both NME and NLE commonly manifest forebrain signs due to the predominance of lesions in the prosencephalon. NLE may also cause mid to caudal brainstem signs. The signs associated with NME and NLE typically are rapidly progressive and most commonly include seizures, depression, circling, vestibulocerebellar signs, visual deficits and ultimately death.

Clinical signs with SRMA are characterized by episodes of profound cervical hyperaesthesia, depression and pyrexia. Two forms of SRMA exist, i.e. the 'classic' acute form and the chronic protracted form. In acute SRMA, dogs most commonly present with hyperaesthesia along the vertebral column, cervical rigidity, stiff gait and fever. Affected animals often manifest a hunched posture with profound guarding of the head and neck, sometimes mimicking a cervical intervertebral disc protrusion. Dogs may be in so much pain that any manipulation elicits a painful response. The chronic form of SRMA most often occurs following relapses of acute disease and/or inadequate treatment. Involvement of the motor and proprioceptive systems may lead to variable degrees of paresis and ataxia. Other neurological signs, such as menace deficits, anisocoria or strabismus, may occur with severe disease.

Idiopathic tremor syndrome typically causes fine tremors affecting all four limbs, the head and sometimes the eyes. The tremors tend to worsen with exercise, stress and excitement, but disappear with sleep. Neurological examination typically is normal, although absent menace responses, nystagmus, dysconjugate eye movements, head tilt, nondescript ataxia, hypermetria, body swaying, varying degrees of paresis and, rarely, seizures have been reported. Neurological signs manifest sporadically, often progress over several days and typically remain static if untreated. Clinical complications associated with prolonged tremors include severe hyperthermia, hypoglycaemia, dehydration and anorexia.

Although the idiopathic MEMs are restricted to the CNS, the severity and location of the CNS lesions occasionally produce profound systemic changes (e.g. autonomic changes with brainstem lesions). Due to the acute, progressive nature of the majority of the conditions causing MEM, dogs and cats often present for emergency evaluation, therefore it is essential to formulate an accurate differential diagnosis in order to perform the correct diagnostic investigations.

DIFFERENTIAL DIAGNOSIS

Metabolic derangements; congenital anomalies (decompensating hydrocephalus, Chiari-like malformation); tumours of the meninges (histiocytosis, lymphoma, meningioma); intervertebral disc disease; atlantoaxial subluxation; cerebrovascular accident; head trauma; mycotoxin and neurotoxin ingestion (for idiopathic tremor syndrome and occasionally disseminated GME).

DIAGNOSIS

Key diagnostic tests for MEM include molecular and advanced imaging diagnostics (*Table 79*).

General meningoencephalomyelitis

The differential diagnosis for dogs presented for an acute onset of multifocal CNS signs includes decompensating congenital abnormalities, metabolic derangements, infectious and idiopathic MEM, neoplasia and toxin exposure. Differentiating these disorders may be challenging. Diagnostic testing typically includes a minimum database (CBC, chemistry panel and urinalysis), survey radiographs of the thorax (+/- abdominal ultrasound) to rule out systemic disease and metastatic neoplasia, advanced cross-sectional imaging via CT or MRI and CSF collection and analysis. Although more often utilized for suspected brain tumours, CT-guided brain biopsy and histopathological evaluation of brain tissue may be considered in cases of suspected ME.

CSF analysis is a key component of the neurodiagnostic work-up and typically includes cytological evaluation, differential cell counts and TP measurement (*Table 80*). While pleocytosis is commonly present in cases of MEM, cytology rarely provides definitive differentiation among idiopathic, infectious and neoplastic disorders. On occasion, bacteria, fungi, protozoa or parasites may be identified on microscopic examination of CSF (see Chapter 5); however, this is extremely rare. One must be especially cautious not to 'overinterpret' the CSF profile. For example, in confirmed cases of MEM, CSF analysis occasionally reveals no abnormalities. Despite its limitations, the CSF WBC differential may help the clinician to narrow down the differential diagnosis, especially when combined with cross-sectional imaging of the CNS.

Table 79 **Diagnostic tests for meningoencephalomyelitis**

DISEASE	DIAGNOSTIC TESTS
Infectious MEM	
Bacterial meningitis	CSF analysis/culture; eubacterial PCR; urine culture
CNS abscess	CSF analysis/culture; eubacterial PCR; urine culture; CT/MRI
Canine distemper virus	PCR of CSF, urine or conjunctival scraping; IHC of skin biopsy; CSF and serum IgM and IgG ratios
FIP	CSF analysis; RT-PCR of CSF or cavitary fluid; CT/MRI, biopsy
Rickettsia rickettsii	Antibody titres; CSF analysis; PCR
Ehrlichia canis	Antibody titres; CSF analysis; PCR
Rabies virus	IFA – postmortem examination
Toxoplasma/Neospora	Antibody titres; CSF analysis; PCR
Cyrptococcus neoformans	Latex agglutination antigen test; CSF analysis/culture
Coccidioides immitis	Complement fixation or AGID (antibody); CSF analysis/culture
Blastomyces dermatitidis	Urine antigen assay
Aspergillus spp.	Latex agglutination antigen test
Parasitic MEM	
Dirofilaria immitis	Antigen ELISA, antibody titres (cat), microfilaria identification
Cuterebra larva	Advanced imaging, postmortem examination
Idiopathic MEM	
GME, NME, NLE, MUA	CSF analysis and lymphoma PCR; CT/MRI; biopsy
SRMA	CSF analysis; CSF culture to rule out infection; CT/MRI
Idiopathic tremor syndrome	CSF analysis; CT/MRI

In both acute and chronic SRMA, blood work may show a neutrophilia with a left shift, an increased erythrocyte sedimentation rate and an elevated alpha2-globulin fraction. The majority of affected dogs have elevated IgA levels in both the CSF and serum, a finding that is probably secondary to dysregulation of the immune system. Elevated serum and CSF IgA levels help differentiate SRMA from other idiopathic and infectious canine meningoencephalitides; however, elevated IgA levels may be associated with primary or secondary inflammation. Elevated IgM and/or IgG levels in the CSF have also been documented. More recently, acute phase proteins (APPs), including C-reactive protein (CRP) and alpha2-macroglobulin, have been shown to be elevated consistently in the serum of dogs with SRMA. However, elevation of APPs is not pathognomonic for the disorder and other systemic inflammatory diseases should be included in the differential diagnosis when it is present. Once SRMA has been confirmed, elevated CRP serum concentrations may be used reliably to monitor response to therapy, rather than repeated CSF collection and analysis.

The presence of anti-astrocytic and glial fibrillary acid protein (GFAP) autoantibodies has been documented in the CSF of affected NME dogs. However, similar antibody levels occur in the CSF of dogs with GME, brain tumours and even some clinically normal dogs. The diagnostic utility of autoantibodies in monitoring response to therapy is limited, since anti-GFAP autoantibodies can even be detected during clinically successful immunosuppressive therapies.

While CT may have diagnostic utility in some cases of inflammatory brain disease, MRI is the gold standard neuroimaging modality for MEM. MRI may be especially helpful for differentiating among the idiopathic meningoencephalitides, as it often discloses lesions that are reflective of the gross neuropathologies associated with each disorder. Although there are overlapping clinical and histopathological features among the meningoencephalitides, the topographical distribution of the lesions (e.g. NME versus NLE) and presence or absence of necrosis (e.g. NME versus GME) may be imaging features that help direct a presumptive antemortem diagnosis. In a recent MRI study, 17/18 Pug dogs with NME had forebrain lesions, with 16/18 having a lesion in the parietal, temporal and occipital lobes. Also, all the Pugs

had asymmetric lesions in both the grey and white matter of the neuroparenchyma. MRI also has several advantages over CT as it provides excellent anatomical detail (especially of the caudal fossa) and allows for acquisition of images in multiple planes (sagittal, transverse, dorsal). Despite the limited soft tissue detail provided by CT, when coupled with CSF analysis it may help to provide evidence of MEM.

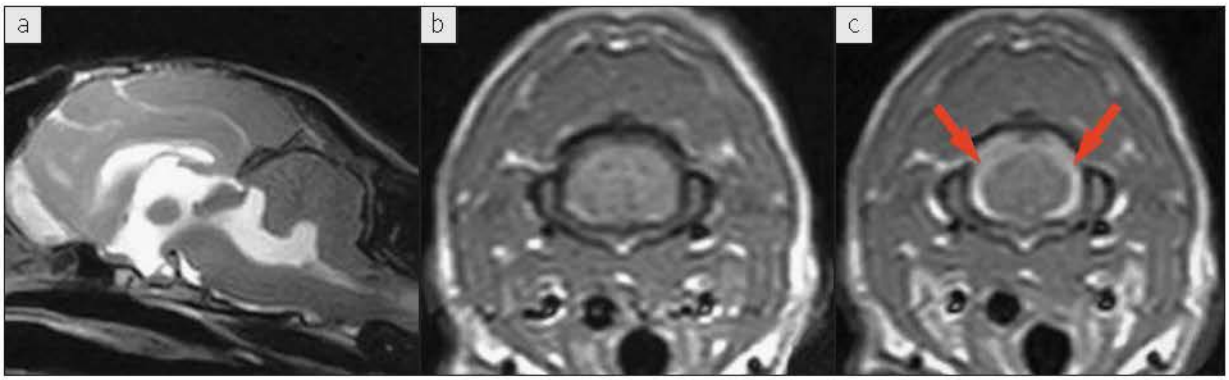
Infectious meningoencephalomyelitis

Traditional techniques to diagnose infectious CNS diseases in dogs and cats include CSF analysis, microbial culture, serological antibody titres, immunohistochemistry (IHC), immunofluorescent antibody (IFA), ELISA and agar gel immunodiffusion (AGID). Identification of infectious organisms on cytology is rare; microbial culture should be considered in cases with systemic signs, potential sources of infection (e.g. otitis media/interna) and CBC/biochemistry abnormalities (e.g. fever, leucocytosis). CSF fungal culture may also be considered in cases with concurrent systemic signs (skin, bone, ocular, internal organ involvement).

Serology and/or PCR should be performed when infectious agents are suspected to be the cause of MEM.

Table 80 **CSF analysis findings in canine and feline CNS disease**

	TOTAL PROTEIN LEVEL	NUCLEATED CELL COUNT	CYTOLOGY
Viral meningoencephalitis (CDV and other)	Normal–markedly elevated	Normal–moderate pleocytosis	Mononuclear
Bacterial meningoencephalitis	Mildy–markedly elevated	Moderate–marked pleocytosis	Predominantly neutrophilic
Protozoal meningoencephalitis	Mildy–markedly elevated	Moderate pleocytosis	Mixed, occasionally eosinophilic
Fungal meningoencephalitis	Markedly elevated	Moderate–marked pleocytosis	Mixed, occasionally eosinophilic
CNS parasites	Mildy–markedly elevated	Mild–moderate pleocytosis	Mixed, often eosinophilic
Granulomatous meningoencephalitis	Mildy–markedly elevated	Normal–marked pleocytosis	Variable: mononuclear, mixed, occasionally eosinophilic
Eosinophilic meningoencephalitis	Mildy–markedly elevated	Mild–marked pleocytosis	Eosinophils
Steroid-responsive meningitis–arteritis	Mildy–markedly elevated	Moderate–marked pleocytosis	Acute: neutrophilic; Chronic: mononuclear
Necrotizing meningoencephalitis, or necrotizing leukoencephalitis	Mildy elevated	Mild–marked pleocytosis	Mononuclear
Feline infectious peritonitis infection	Markedly elevated	Moderate–marked pleocytosis	Mixed, occasionally eosinophilic
Neoplasia	Variable: normal–markedly elevated	Variable: normal–marked pleocytosis	Variable: mononuclear, neutrophilic (e.g. meningioma), occasionally eosinophilic or neoplastic cells (e.g. lymphosarcoma)
Degenerative disorders	Normal–moderately elevated	Normal	—
Necrosis	Normal–markedly elevated	Variable: normal–marked pleocytosis	Mixed pleocytosis (often neutrophilic)



▲ 275 (a) Sagittal T2-weighted image of the brain of an 8-month-old cat with the CNS form of FIP. There is marked dilatation of the 3rd and 4th ventricles, with secondary dorsal displacement of the cerebellum and cerebellar vermal herniation through the foramen magnum. The proximal part of the cervical spinal cord appears swollen and hyperintense. (b) Transverse T1-weighted and (c) T1-weighted post-contrast images of the spinal cord at the level of C1. There is marked thickening and contrast enhancement of the meninges surrounding the spinal cord (arrows), which probably accounts for the secondary obstructive hydrocephalus. FIP is a surface-related disease affecting mostly the leptomeninges and ependymal lining of the CNS. (Photo courtesy Laurent Garosi)

IgM and IgG antibodies reflect acute and chronic infections, respectively, and can be evaluated in the serum and/or CSF. Although positive antibody titres reflect direct exposure to an organism, a positive titre does not confirm active infection. Serology results must be interpreted in light of the patient's signalment, history, neurological and systemic signs, CSF analysis and imaging results. Serum and CSF serology and PCR may be pursued for *Toxoplasma gondii* (IgG and IgM ELISA, PCR), *Neospora caninum* (IgG indirect IFA, PCR), *Ehrlichia* spp. (IgG indirect IFA, PCR) and *Rickettsia rickettsii* (IgG IFA, PCR). AGID panels and panfungal PCR are available for *Cryptococcus*, *Blastomyces*, *Coccidioides*, and *Histoplasma* spp. Eubacterial PCR detection of 16S ribosomal subunits is currently being investigated.

Biopsy and IHC are required for the definitive diagnosis of FIP. However, a presumptive antemortem diagnosis can be achieved with CSF analysis and MRI. CSF analysis typically reveals protein levels of 2 g/l (200 mg/dl) or greater and a moderate to marked neutrophilic pleocytosis. MRI may reveal periventricular contrast enhancement, ventricular dilatation and/or hydrocephalus (**275**). Reverse transcription PCR of FIP virus in infected macrophages has been reported; however, false positives may occur in healthy cats .

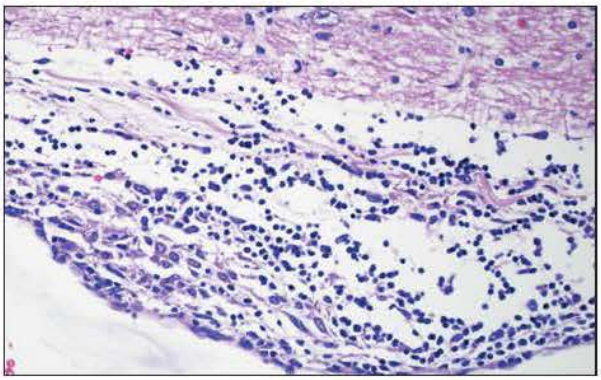
Since CSF and MRI findings are highly variable with CDV infection, diagnostic techniques with greater specificity must be utilized. Immunohistochemical testing for CDV antigen on biopsies of nasal mucosa, footpad epithelium and the haired skin of the dorsal neck has been reported to be a relatively sensitive and specific test. Similarly, reverse transcription PCR applied to RNA extracted from whole blood, urine, CSF, tonsilar or conjunctival specimens is a sensitive and specific assay.

Idiopathic meningoencephalomyelitis

A definitive antemortem diagnosis of the specific variants of idiopathic MEM is challenging, since histopathological confirmation is required (**276**). In most cases a presumptive antemortem diagnosis is achieved via a multimodal approach that includes assessment of case signalment, neurological signs and neuroanatomical localization, CSF analysis, cross-sectional imaging of the CNS and negative infectious disease testing. The antemortem diagnosis is often complicated by an overlap in the neurodiagnostic profiles (especially between GME and the necrotizing encephalitides). Therefore, the terminology meningoencephalitis of unknown aetiology (MUA) may be preferable on an antemortem basis in cases of idiopathic ME where histopathology is lacking.

The following points regarding CSF analysis (see also *Table 80*) and cross-sectional imaging may help with presumptive diagnoses of the idiopathic MEMs:

- The CSF profiles for GME, NME, NLE and chronic SRMA overlap, with a mononuclear (lymphocytes, monocytes) pleocytosis and TP elevations being most common.
- The CSF profile for acute SRMA is typified by a neutrophilic pleocytosis, TP elevation and elevated IgA (CSF and serum).
- The CSF profile for idiopathic tremor syndrome is typified by a lymphocytic pleocytosis and TP elevation.
- Although not specific for GME, the most common MRI findings for the disseminated form include multiple hyperintensities on T2-weighted or FLAIR sequences scattered throughout the CNS white matter. These lesions typically assume an infiltrative appearance and have irregular margins.
- Despite the predilection of the GME for white matter, MRI lesions are often distributed throughout both grey and white matter. Compared with cerebral parenchyma, the lesions are hyperintense on T2-weighted images, variable intensity on T1-weighted images and have variable degrees of contrast enhancement. Vasogenic oedema in the white matter is commonly appreciable on T2-weighted and T1-weighted images as hyper- and hypointense to cerebral parenchyma, respectively.
- Both focal and disseminated forms of GME may be associated with contrast enhancement of the parenchyma and meninges on CT, and mass effect may be observed as displacement of surrounding brain tissue. Some lesions may be associated with hypoattenuating vasogenic (white matter) oedema.
- The focal form of GME may be identified on CT or MRI as a nonspecific, single, space-occupying mass lesion.
- In ocular GME, the optic nerves may be hyperintense on T2-weighted images and may show contrast enhancement on T1-weighted images. The optic chiasm also may appear enlarged, reflecting the gross pathology.
- Mild NME, infectious ME, CNS lymphosarcoma and glial and metastatic neoplasms may present with similar clinical and MRI findings to disseminated GME, and discriminating among these differentials may be challenging unless tissue biopsy is obtained.
- Typical MRI lesions associated with NME include asymmetric, multifocal prosencephalic lesions affecting the grey and white matter, with variable contrast enhancement on T1-weighted imaging. Loss of grey/white matter demarcation also may be discernible. Lesions appear hyperintense on T2-weighted images and isointense to slightly hypointense on T1-weighted images, with slight contrast enhancement.



▲ **276** **Histopathology of the brain and meningeal tissue from a canine case of GME (× 20), which demonstrates the cellular accumulation within the meninges often evident in these cases. (Photo courtesy Victoria Watson)**

- In NLE, multiple, asymmetric bilateral prosencephalic lesions mainly affecting the subcortical white matter have been described. The NLE lesions are hyperintense on T2-weighted and FLAIR images and often include multiple cystic areas of necrosis. These lesions are hypointense or isointense on T1-weighted images, and contrast enhancement is variable.
- Although leptomeningeal enhancement may be appreciated on CT or MRI with SRMA or idiopathic tremor syndrome, cross-sectional imaging typically is normal for both disorders.

MANAGEMENT

Infectious meningoencephalomyelitis

Treatment of bacterial meningitis and CNS abscesses necessitates the selection of an antibiotic that effectively crosses the blood–brain/CSF barrier. Antibiotic selection should be based on culture and sensitivity results if available. Empirical antibiotics should initially be given intravenously for 2–3 days to reach therapeutic levels in a timely manner. Antibiotic choices include trimethoprim sulphonamide (30–60 mg/kg q24h) and metronidazole (10–15 mg/kg q12h). Other choices include third-generation cephalosporins and fluoroquinolones such as enrofloxacin (5–10 mg/kg q24h). Antibiotics should be continued for 3–4 weeks after clinical signs have resolved. Intravenous dexamethasone (0.05–0.1 mg/kg q24h) can be given for the first 24–48 hours to decrease vasogenic oedema. Increased ICP may be seen with large CNS abscesses (see below for treatment of increased ICP). Abscesses of the CNS may be refractory to treatment due to the fibrous capsule. Surgical decompression by craniotomy, burr holes or laminectomy may be indicated in cases of cranial subdural or spinal epidural empyema.

To date, there is no definitive treatment for viral ME. Supportive treatment and broad-spectrum antibiotics are given to prevent secondary bacterial infections in cases of CDV and FIP infection. Anti-inflammatory corticosteroids may reduce inflammation in dogs or cats with any suspected viral ME. Euthanasia is recommended for all animals with a history and clinical signs supportive of rabies infection. In addition, rabies is a notifiable disease in some countries and appropriate measures to inform the relevant authorities should be taken.

For toxoplasmosis or neosporosis, clindamycin (10–25 mg/kg IV initially, then PO q12h for 3–4 weeks) may lead to a favourable outcome. Trimethoprim sulphonamide (15 mg/kg PO q12h) in combination with pyrimethamine (1 mg/kg/day PO) may also be effective. Folinic acid or brewers yeast supplementation should be considered (5 mg/dog q24h) in animals receiving this latter therapy. However, bradyzoite cysts may not be affected by antibiotics, resulting in disease recrudescence during periods of immunosuppression, with possible initiation of clinical signs. Rickettsial organisms should be treated with doxycycline (5–10 mg/kg q12h for 4–6 weeks). Fungal MEM may be treated with voriconazole (40–60 mg/kg PO q24h). Cryptococcal infections are often treated with a combination of fluconazole (2.5–5.0 mg/kg PO) and amphotericin B (0.5–0.8 mg/kg SC [diluted in 0.45% NaCl with 2.5% dextrose]) 2–3 times per week (**277**, next page).

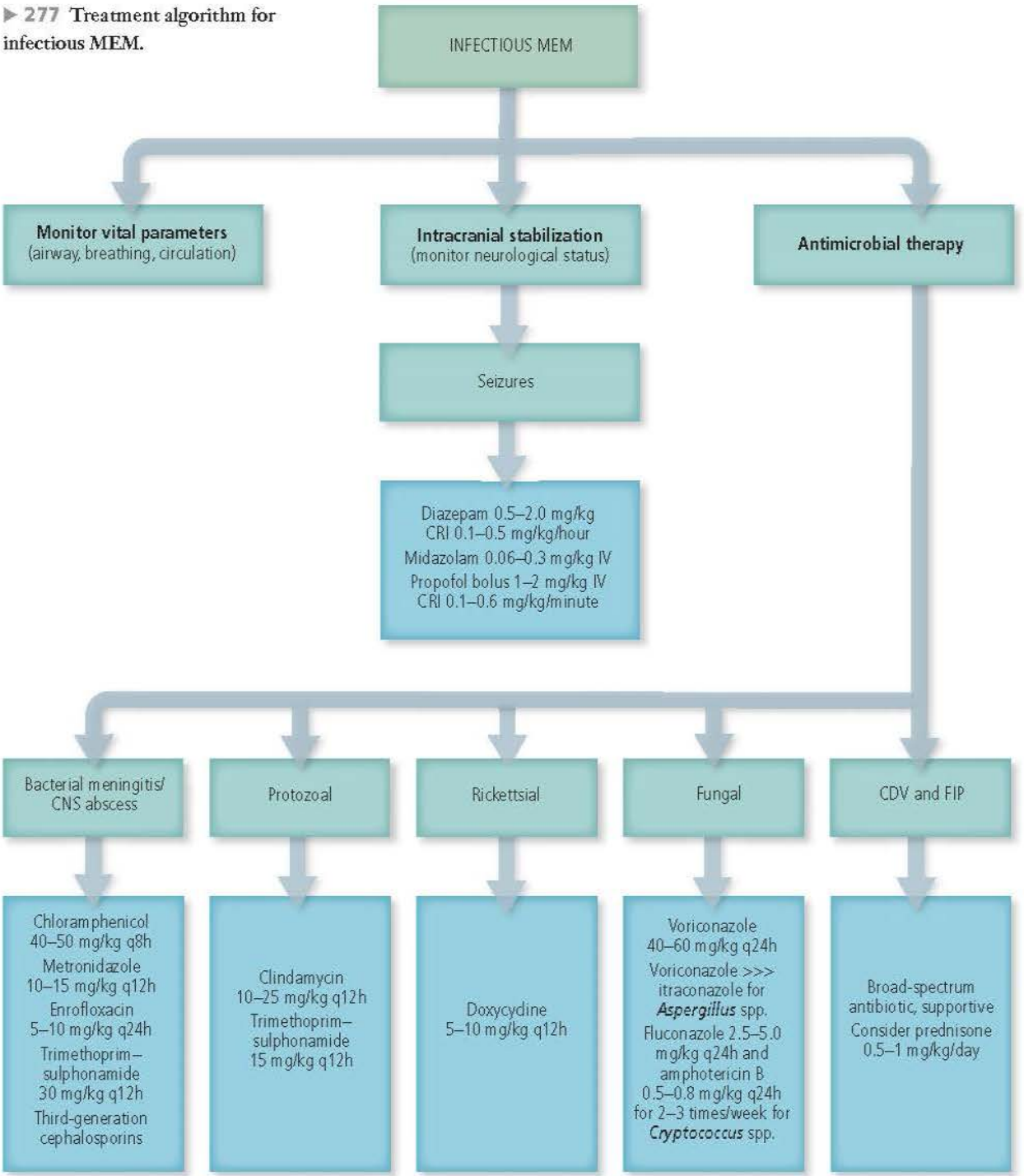
Anti-inflammatory doses of corticosteroids can be given in some cases of infectious MEM in which vasogenic oedema and/or an immune-mediated component of the disease process is present. Dexamethasone (0.05–0.1 mg/kg IV q24h for the first 24–48 hours) followed by prednisolone (0.5–1.0 mg/kg PO q24h for 1–2 weeks) can be used in the acute setting of infectious MEM.

Idiopathic meningoencephalomyelitis (GME, NME, NLE, MUA)

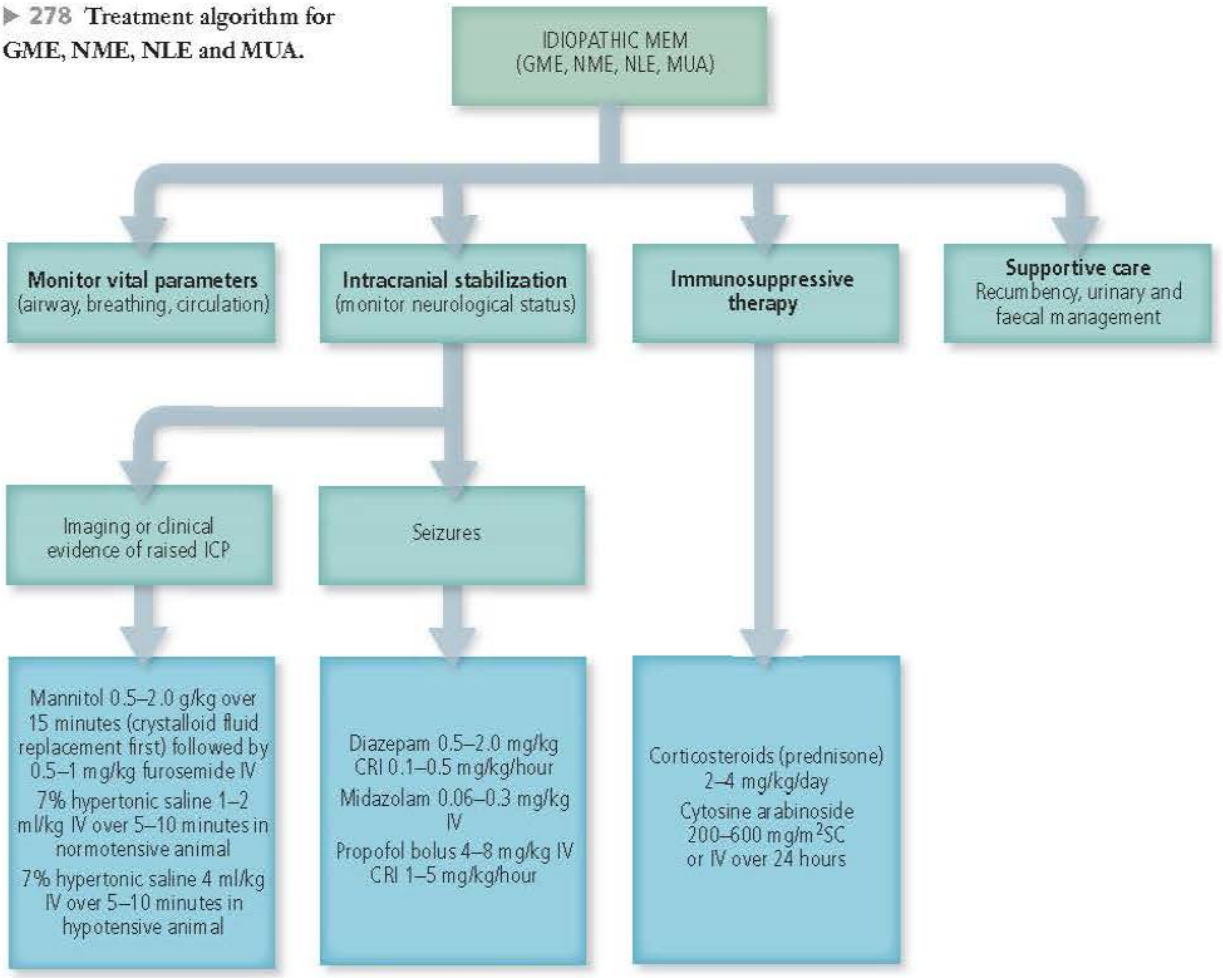
The primary therapy for idiopathic MEM is immunosuppression with corticosteroids and secondary immunosuppressive agents.

Once an infectious aetiology has been ruled out and a presumptive or definitive diagnosis of idiopathic MEM reached, treatment should be instituted as soon as possible. The patient should initially be stabilized if neurological derangements have produced respiratory or cardiovascular abnormalities (e.g. seizures or brainstem lesions causing secondary autonomic changes). Supplementary oxygen should be given for hypoxaemia and crystalloid/colloid support for perfusion and hypotension, as needed. Once systemic parameters are stabilized, therapy should be instituted (1) to prevent neurological deterioration, (2) to halt the immune response with immunosuppressive therapy and (3) to provide support for a recumbent patient if needed (**278**, page 359).

▶ **277** **Treatment algorithm for infectious MEM.**



▶ 278 Treatment algorithm for GME, NME, NLE and MUA.



Preventing neurological deterioration

If seizures are present, diazepam or midazolam may be given. (For control of emergency seizures see Chapter 23.) If neurological status progressively worsens and increased ICP is suspected, mannitol may be given through an in-line filter. Some clinicians recommend mannitol dosing every 30 minutes until the desired effect has been achieved. Intravenous furosemide may also be given following mannitol administration. The patient must be adequately hydrated before mannitol is given in order to prevent hypovolaemia and potential renal damage. An alternative to mannitol is hypertonic saline. (See Chapters 20 and 26 for management of elevated ICP.)

Halting the immune response with immunosuppressive therapy

At present, immunosuppression is the mainstay of therapy for MUA. Most clinicians treat MUA with corticosteroids (prednisone or dexamethasone). In a large study of dogs with GME, radiation therapy appeared to be the only independent predictor of patient survival. However, these results may be biased, as patient inclusion was based on only necropsied GME dogs. Depending on the severity of signs and the index of suspicion for infectious disease, some specialists will initiate therapy with anti-inflammatory steroids (prednisone, 0.5–1.0 mg/kg PO q24h) and await serology and PCR results for screening of regional infectious diseases.

If the index of suspicion is extremely high for idiopathic inflammatory disease (e.g. Pug with MRI lesions consistent with NME), the authors immediately initiate immunosuppressive therapy. Response to corticosteroids is variable and may be temporary, but dogs often have a favourable initial response to steroid monotherapy. Additional immunosuppression is considered on a case-by-case basis, but the authors typically use secondary immunomodulatory agents on review of negative serology and PCR results.

In a clinical setting, steroid monotherapy may resolve signs associated with MUA in some dogs, but insufficiently or only transiently provide resolution in others. Moreover, long-term, high-dose corticosteroid therapy often causes adverse effects including polyuria/polydipsia, polyphagia, weight gain, hepatotoxicity, gastrointestinal ulceration, pancreatitis and iatrogenic hyperadrenocorticism. These combined factors have led to a recent focus on additional immunomodulatory drugs to treat MUA (e.g. cytosine arabinoside [CA], 50 mg/m^2 SC q12h for 2 days [see *Table 81*]; procarbazine, 25–50 mg/m^2 PO q24h; cyclosporine, 5–10 mg/kg PO q12h; azathioprine, 2 mg/kg PO q24h; mycophenolate, 10–20 mg/kg PO q12h; and leflunomide, 2–4 mg/kg PO q24). In a recent study, patient survival times and adverse effects were compared between a prednisone/vincristine/cyclophosphamide protocol and a prednisone/CA protocol. There was no significant difference between survival times between the two groups. Adverse effects were seen more often in the cyclophosphamide group. The authors commonly use CA as an adjunctive therapy for MUA in combination with prednisone using the following protocol:

- 1.5 mg/kg q12h for 3 weeks;
- 1.0 mg/kg q12h for 6 weeks;
- 0.5 mg/kg q12h for 3 weeks;
- 0.5 mg/kg q24h for 3 weeks;
- 0.5 mg/kg q48h indefinitely (may reduce to 0.25 mg/kg q48h).

Intravenous rescue CA protocols (IV CRI at 200 mg/m^2 over 48 hours) have been described for the initial treatment of severe idiopathic MEM. The authors have also used a higher intravenous dose regimen (600 mg/m^2 over 24–48 hours), which seems to be useful for severe relapses. It is recommended that intravenous rescue CA protocols are used in severely affected dogs.

Table 81 **Cytosine arabinoside regimen for idiopathic meningoencephalomyelitis**

Intervals between treatment*	Dosages given on consecutive days	Number of treatments
3 weeks apart	50 mg/m^2 SC q12h x 2 days	4
4 weeks apart	50 mg/m^2 SC q12h x 2 days	4
5 weeks apart	50 mg/m^2 SC q12h x 2 days	4
6 weeks apart	50 mg/m^2 SC q12h x 2 days	Indefinitely

Intervals between doses can be adjusted based on clinical response and occasionally repeat CSF analysis and MRI.

* Treatment interval should only be extended if the patient remains in clinical remission. If clinical signs recur, the last effective treatment interval should be used indefinitely. At the 6-week stage, an attempt to take the dog off CA can be made based on clinical response.

Treatment is monitored by clinical response and regression of neurological deficits and occasionally repeated CSF analysis and MRI. In our experience, side-effects have been minimal and dogs with MUA have a fair long-term prognosis with combined CA/prednisone therapy. However, CBCs are evaluated 10–14 days after the first dosing regimen, then every 2–3 months to monitor myeloid cell lines.

Providing support for a recumbent patient

Recumbent patients need to be properly managed to prevent bed sores and urine scald. Ideally, the recumbency of the patient and appropriate urinary and faecal management need to be addressed every 4–6 hours. Urine and faeces must be cleaned off the patient as soon as possible in order to prevent dermatitis. Occasionally, recumbent and, sometimes, demented patients may need fluid therapy to support base fluid requirement and compensate for corticosteroid-induced polyuria.

Idiopathic meningoencephalomyelitis (presumptive SRMA and idiopathic tremor syndrome)

Immunosuppressive doses of corticosteroids form the cornerstone of therapy for SRMA and idiopathic tremor syndrome. For SRMA, the following protocol has been recommended for a minimum of 6 months:

- Prednisone (2 mg/kg PO or IV initially q12h). After 2 days the dose is reduced to 1 mg/kg PO q12h for 1–2 weeks, followed by 0.5 mg/kg PO q12h.
- Dogs are re-examined every 4–6 weeks; CSF analysis and haematology can be repeated every 4–6 weeks.
- When clinical signs and/or CSF are normal, the dose is reduced by half until a dose of 0.5 mg/kg q48–72h is reached.
- Treatment is stopped 6 months after clinical examination and CSF evaluation are normal.
- For chronic or refractory cases, other immunosuppressive drugs, such as azathioprine (1.5–2.0 mg/kg PO q48h), may be used in combination with steroids (e.g. alternating each drug every other day).

The majority of dogs with idiopathic tremor syndrome respond to corticosteroid immunosuppression within 3 days. The duration of steroid therapy may range from 4 weeks to several months. For refractory cases of idiopathic tremor syndrome, diazepam (0.5 mg/kg PO q8h) or propanolol (2.5–10 mg/dog PO q8–12h) may be instituted. The rationale for propanolol treatment is based on the observation that catecholamines enhance physiological tremors in humans; therefore, beta-adrenergic antagonism of receptors in muscle and CNS may ameliorate tremors. Cyclosporine has also been reported anecdotally to be a useful adjunctive therapy for idiopathic tremor syndrome.

PROGNOSIS

Infectious meningoencephalomyelitis

The prognosis for infectious MEM (bacterial, CDV, protozoal, fungal) is dependent on the aetiology, duration, recrudescence of disease and severity of neurological signs. Rabies MEM is associated with a grave prognosis, as animals infected with rabies typically succumb to the disease within 3–10 days of initial neurological signs. The mortality rate for cats affected with CNS FIP is nearly 100%, with survival times ranging from weeks to months.

Idiopathic meningoencephalomyelitis

The prognosis for GME is considered to be poor without aggressive immunosuppression. The largest study of histopathologically confirmed GME cases included 42 dogs with survival times ranging from 1 to >1,215 days. The major factors affecting survival were neuroanatomical localization and focal versus multifocal neurological signs. Dogs with focal GME were reported to survive longer (median 114 days) than those with the disseminated form, which died within a few days to weeks (median 8 days) of diagnosis. This large study suggests that GME has a poor prognosis, with most dogs succumbing to the disorder or being euthanized within a few weeks to months after diagnosis, despite steroid treatment. However, the study was limited to post-mortem confirmed disease, so survival times and the associated prognosis may be biased towards dogs with severe GME.

A recent epidemiological study of Pugs with NME disclosed a median survival of 93 days (range, 1–680 days), with dogs receiving any form of treatment living significantly longer than those that were not treated. The prognosis for SRMA is fair to good, especially for dogs with acute disease that are treated with aggressive immunosuppression. Untreated dogs typically have a relapsing and remitting disease course. The prognosis for idiopathic tremor syndrome is generally favourable. Tremors typically abate in most dogs by the end of the first week of therapy. Some dogs relapse at the end of the treatment, requiring continued or adjunctive immunosuppressive therapy. Occasionally, relapses may occur after several months or years. Re-institution of prednisone therapy typically results in resolution of tremors within 5 days in relapsing cases.

Previous reports of combined prednisone and CA treatment protocols for MUA showed survival times of 46–1,025 days. In a more recent study comparing prednisone/vincristine/cyclophosphamide with prednisone /CA protocols for treatment of MUA, median survival times did not differ between the groups and were both >12 months. Side-effects with the cyclophosphamide

protocol were greater and more severe than with the CA protocol. Cyclosporine has also been evaluated for the treatment of MUA, with an overall median survival time (10 dogs) of 930 days (range, 60–1,290 days). Side-effects were minimal and included excessive shedding, gingival hyperplasia and hypertrichosis. The median survival time of 40 dogs with presumed MUA treated with prednisone and azathioprine was 1,834 days (range, 50–2,469 days). Finally, in a study of dogs with MUA comparing dogs treated with procarbazine and prednisone with dogs not receiving any treatment, median survival time was 14 months and 0.73 months, respectively.

HEAD TRAUMA

Courtenay Freeman & Simon Platt

INTRODUCTION

Head trauma is an important cause of morbidity and mortality in both humans and animals. Immediate and appropriate treatment is critical to potentiate an acceptable recovery. Although treatment recommendations in veterinary medicine remain controversial, there are several guidelines for head trauma management. Accurate and frequent assessment of both systemic and neurological injuries can allow for a successful outcome. Additionally, treatment strategies should remain flexible, adjusting to the patient's needs and changes in neurological status. A complete understanding of intracranial physiology and the effects of injury will aid in the management of dogs and cats with head trauma.

The following definitions are useful when discussing head trauma in small animals:

- **ICP** is the pressure exerted within the skull by the intracranial contents. Normal ICP in a dog is between 5 and 12 mmHg.
- **CPP**, the pressure of blood flowing to the brain, is reliant on a balance between MAP and ICP: CPP = MAP minus ICP. Elevations in ICP can have a significant impact on CPP, leading to decreased brain perfusion.
- **CBF** is the rate of blood delivery into the brain and is driven predominantly by CPP. CBF is regulated by cerebral metabolic activity, partial pressure of oxygen and partial pressure of carbon dioxide. The relationship between CPP, CBF and cerebral vascular resistance (CVR) is CBF = CPP/CVR. CVR depends primarily on blood viscosity and vessel diameter.
- **Autoregulation** is the intrinsic ability of the brain to maintain cerebral perfusion.
- **Compliance** is the ability of the intracranial contents to decrease in volume in an attempt to maintain normal ICP.
- **Concussion** is a reversible traumatic paralysis of nervous system function and is immediate in onset. The effects of concussion on brain function may last for a variable amount of time. This term does not describe underlying brain pathology.
- **Contusion** is a common result of severe head injury, often associated with a concussion. It represents a bruising of the brain surface without rupture of the pia-arachnoid and/or interruption of the brain architecture.

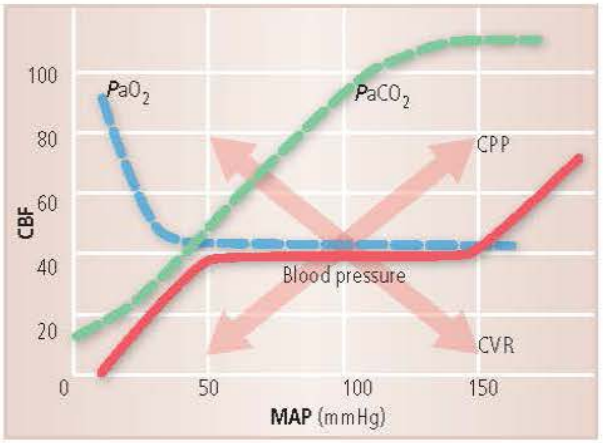
AETIOLOGY AND PATHOPHYSIOLOGY

Traumatic brain injury in veterinary patients occurs most commonly secondary to road traffic accidents. Other common causes of traumatic brain injury include kicks to the head, falls, gunshot wounds and animal bites.

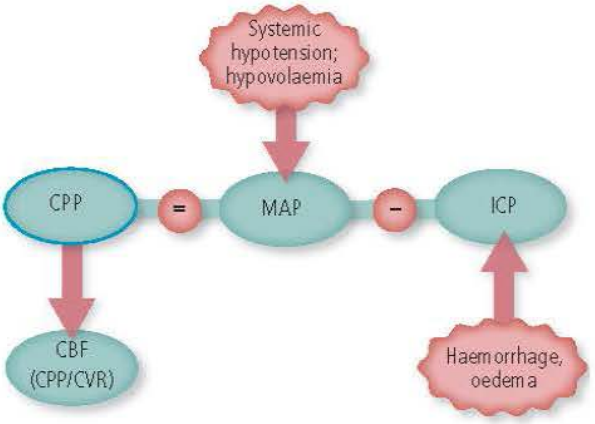
Normal physiology

The brain receives 15–20% of the total cardiac output with each cardiac cycle. The high metabolic rate and dependence of the brain on adequate circulation for nutrients demonstrate the need for adequate blood flow. CBF is driven by systemic arterial pressure, but is dependent on several factors. BP, cerebral metabolic rates, blood oxygen levels and carbon dioxide levels have a significant effect on CBF.

The brain has an intrinsic ability to maintain CBF despite fluctuations in CPP. This ability is known as autoregulation. Autoregulation is mediated through myogenic, chemical and neurogenic mechanisms maintaining tight control over CVR. Myogenic factors



▲ 279 The relationship between cerebral blood flow (CBF), arterial oxygen and carbon dioxide levels and mean arterial blood pressure (MAP). CBF is maintained at a constant throughout wide variations in MAP (autoregulation), which is primarily due to an inverse relationship between cerebral perfusion pressure (CPP) and cerebral vascular resistance (CVR) or vascular diameter.



▲ 280 The relationship between cerebral perfusion pressure (CPP), mean arterial blood pressure (MAP) and intracranial pressure (ICP) is tightly regulated, but can be affected by various pathologies and systemic disturbances. CPP is shown here to be responsible for CBF, which can only be kept constant by alteration of the cerebral vascular resistance (CVR).

describe the ability of the vascular smooth muscle to contract or dilate in response to arterial pressure; a constant CBF occurs between MAPs of 50 and 150 mmHg (**279**). Outside of this range, blood flow to the brain will be dependent on systemic arterial circulation. Chemical factors mediating autoregulation include: oxygen, with a decrease in arterial concentration resulting in vasodilation and vice versa; carbon dioxide, with an increase in arterial concentration resulting in vasodilation and vice versa; and nitric oxide. Finally, the sympathetic and parasympathetic innervations of the vasculature allow for further neurogenic control over blood flow to the brain. A functional and intact blood–brain barrier is required for proper function of autoregulation. Therefore, loss of autoregulation following head trauma is related to disruption of the blood–brain barrier and a decline in CPP. Failure of autoregulation allows CBF to passively follow arterial pressure and be less responsive to changes in oxygen delivery.

CPP is defined as the difference between MAP and ICP and an elevation in ICP and/or a drop in MAP leads to decreased CPP. Ischaemia and a loss of autoregulation occur with a CPP <40 mmHg. The relationship between CPP, CBF and CVR is CBF = CPP/CVR. CVR depends primarily on blood viscosity and vessel diameter, therefore CBF is kept constant by fluctuations in CVR to compensate for alterations in CPP, which can occur due to MAP changes (**279**).

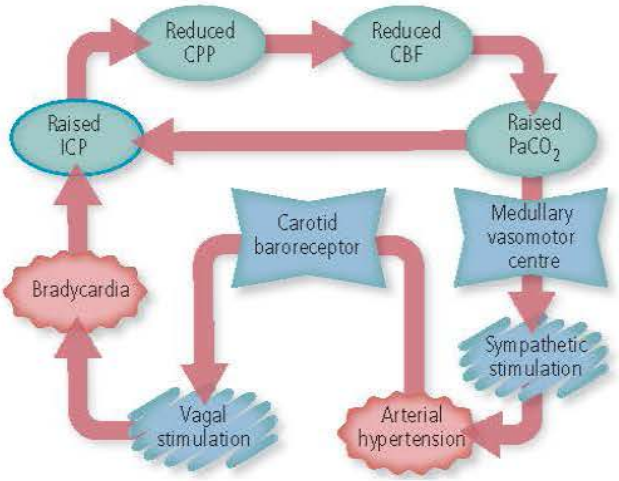
Injury-related physiology

Following injury, CBF is often significantly reduced due to associated elevations in ICP (≥12–20 mmHg). Specific factors that decrease CBF include the presence of oedema, haematomas, compression of vessels from mass effect and vasospasm. Additionally, trauma significant enough to cause brain injury probably causes some degree of systemic shock and hypotension. The presence of hypotension further reduces cerebral blood flow (**280**).

Reduction in CBF due to raised ICP can lead to brain ischaemia. A series of physiological responses, when CBF declines, are in place to prevent this. Reduced blood flow to the vasomotor centres in the brainstem leads to reduced carbon dioxide removal. Subsequent elevation in local carbon dioxide concentrations stimulates the

sympathetic nervous system to increase MAP. The result is systemic hypertension in an effort to maintain blood flow to the brain. However, as the baroreceptors located in the aorta and carotid sinus both detect systemic hypertension, a signal is sent to the vagal centres of the brainstem. A reflex bradycardia occurs as a consequence. This phenomenon is referred to as the Cushing reflex (**281**). Therefore, concurrent systemic hypertension and bradycardia can indicate elevated ICP in head trauma patients.

Additionally, an elevation in ICP and the subsequent reduction in CPP stimulate the release of catecholamines. This catecholamine surge can lead to the brain–heart syndrome, which causes arrhythmias and myocardial ischaemia.



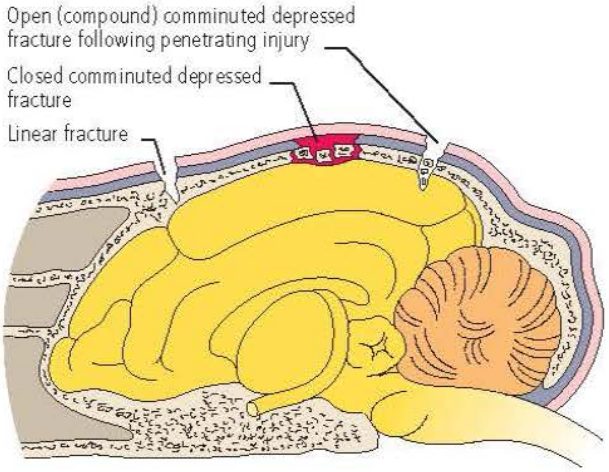
▲ 281 **The Cushing reflex creates a hypertensive and bradycardic response to raised intracranial pressure (ICP) as reduced cerebral perfusion pressure (CPP) and cerebral blood flow (CBF) result in elevated CO_2 concentrations.**

Primary and secondary brain injury

After trauma, the brain parenchyma is susceptible to two types of injury: primary injury and secondary injury.

Primary injury

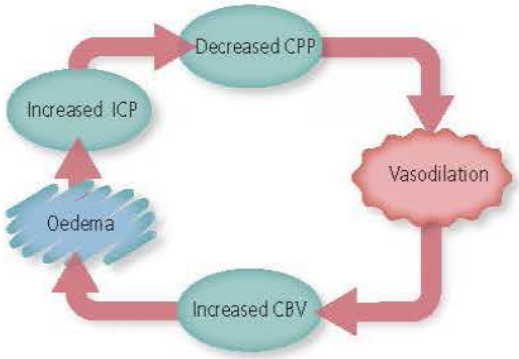
Primary, or biomechanical injury, describes the injury to the brain tissue from direct trauma and the forces applied to the brain at impact. An impact to the skull exerts the following forces on the brain: acceleration, deceleration and rotational forces. The brain is unable to tolerate these forces because of its composition and lack of internal support. The superficial grey matter is most susceptible to the forces of acceleration, leading to haemorrhage or contusion and tearing of neuronal tissue. The rotational forces have more of an impact on the deeper white matter of the brain, causing concussive injuries and axonal damage. The roughly spherical shape of the skull and the propagation of rotational forces after injury direct these forces into the deeper tissues of the brain. Additionally, penetrating injuries can cause fractures, haemorrhage and direct damage to the brain parenchyma.



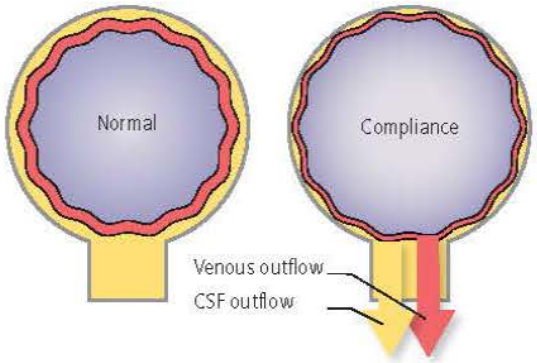
▲ 282 **Fracture classification of the calvarium.**

Skull fractures

Skull fractures are described based on pattern (depressed, comminuted, linear [**282**]), location and type (open versus closed). A depressed fracture is one where the inner shelf of bone is driven into the brain to a depth equivalent to the width of the skull. Depressed fractures are most common on the dorsal and lateral aspects of the skull. Fractures may also occur at the base of the skull, the middle ear and the temporomandibular joint; however, fractures in these locations are difficult to evaluate. Bullae fractures can result in neurological signs such as vestibular syndrome, facial paresis/paralysis and Horner's syndrome on the side of the fracture. Fractures of the temporomandibular joint, mandible and zygomatic arch may require additional treatment, but are unlikely to cause neurological signs alone.



▲ 284 The vasodilatory cascade and its relationship with oedema. Vasodilation occurs in response to a decreased cerebral perfusion pressure (CPP). This increases cerebral blood volume (CBV), which in turn exacerbates oedema and increases intracranial pressure (ICP).

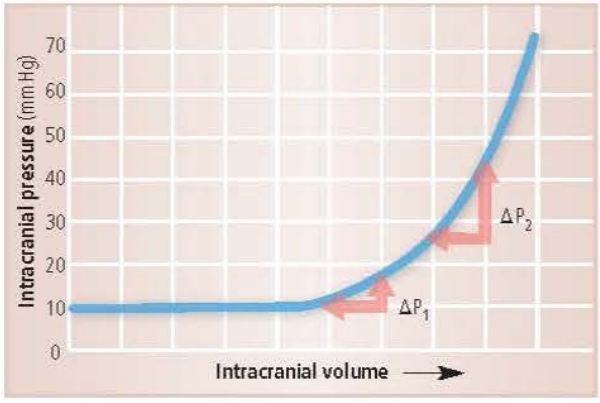


▲ 285 The Monro–Kellie doctrine describes the ability of the intracranial cavity and its contents to maintain a relatively constant intracranial pressure when its volume increases. This is possible due to compliance, whereby CSF is shunted out of the intracranial cavity and, subsequently, vasoconstriction decreases cerebral blood volume.

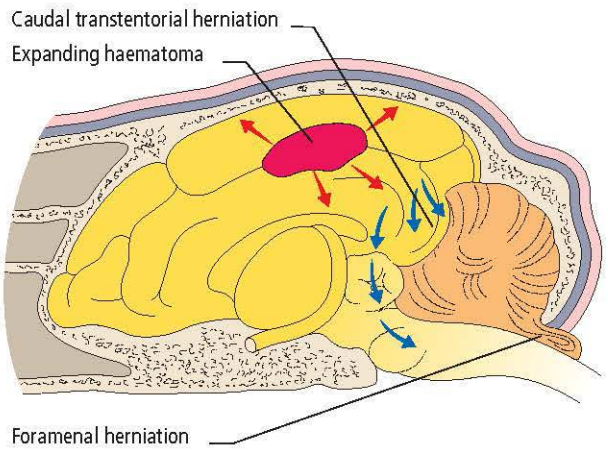
Intracranial pressure

The brain is protected within the bony confines of the skull, where it exists in equilibrium with CSF and blood. The pressure exerted between the brain and the skull is the ICP, which is normally between 5 and 12 mmHg in dogs and cats. The skull is relatively inelastic, limiting the volume that can exist within the cranial cavity. The space within the cranial vault is occupied primarily by three components: brain parenchyma, CSF and blood.

The Monro–Kellie doctrine describes the relationship between these components and their ability to compensate for increases in volume within the cranial cavity (**285**). After head trauma, the volume of the intracranial contents within the skull may increase due to haemorrhage, oedema or CSF accumulation. The brain has the capacity to tolerate small increases in volume by adjusting the size of one of the three components, primarily CSF. Shunting CSF to the spinal subarachnoid space, decreasing CSF production and increasing CSF absorption can rapidly decrease the intracranial CSF volume. CSF production does not typically effect elevations in ICP unless its drainage is obstructed, leading to obstructive hydrocephalus. Additionally, venous blood can be redirected out of the cranial cavity and CBF will decrease to compensate for ICP elevation. The ability of the brain to adjust for increases in ICP by decreasing the volume of CSF and blood is called compliance. During this time of compensation, the patient's clinical signs will remain relatively normal, unless the trauma primarily injured the parenchyma (e.g. laceration, puncture wounds). Once compliance is exhausted, small increases in volume will result in dramatic elevations in ICP, which will be accompanied by a rapid decline in the patient's neurological status (**286**). This ability to compensate is more effective if the increase in volume occurs slowly. With continued elevation of ICP, brain herniation can result.



▲ 286 As intracranial volume increases, compliance ensures that the intracranial pressure (ICP) remains constant until a point when small increases in volume cause exponential increases in ICP.



▲ **287 Caudal transtentorial herniation occurs when the parahippocampal gyrus of the occipital lobe herniates underneath the osseous tentorium. In foramenal herniation the cerebellar vermis herniates caudally through the foramen magnum.**

There are four types of brain herniation:

- Falcine herniation: herniation of one cerebral hemisphere ventral to the falx cerebri.
- Transtentorial herniation (**287**): herniation of the parahippocampal gyrus below the tentorium cerebelli, which causes compression of the midbrain and leads to mydriatic, unresponsive pupils and loss of consciousness. A sign of developing transtentorial herniation is asymmetric mydriasis followed by symmetrical mydriasis as the parasympathetic portion of the CN III nucleus is compressed. Transtentorial herniation can be life threatening, leading to sudden cardiopulmonary arrest.
- Foramenal herniation: cerebellar herniation into the foramen magnum (**287**). This is frequently fatal, causing respiratory arrest by compressing the respiratory centres of the medulla.
- Calvarial herniation: the brain can also herniate through a defect in the skull.

CLINICAL ASSESSMENT

The ability to recognize signs consistent with elevated ICP or a declining neurological status is critical in the management of dogs and cats following head trauma. Trauma significant enough to cause brain injury will have systemic effects, which may be life threatening, and systemic injuries and shock will cause continued decline. Therefore, complete systemic evaluation and stabilization are required in addition to a thorough neurological assessment (*Table 82*).

Systemic assessment

Initial assessment should involve evaluation of the patient's respiratory and cardiovascular systems. An airway must be established, if necessary through endotracheal intubation. Breathing patterns may be affected by thoracic trauma, but may also be secondary to brain injury. Auscultation of the thorax may detect pulmonary pathology or cardiac arrhythmias. Oxygen support should be given as necessary and mechanical or manual ventilation may be required with severe pulmonary injuries. Traumatic pneumothorax may require thoracocentesis or chest tube placement to allow proper ventilation. The cardiovascular system should be evaluated by monitoring heart rate and BP and by electrocardiography. An ECG may demonstrate cardiac arrhythmias secondary to traumatic myocarditis, systemic shock or brain injury. Arterial blood analysis and lactate concentrations may provide additional information regarding systemic perfusion and respiratory function.

Temperature assessment on a frequent basis is important in all head trauma patients. Cerebral metabolic rate is proportional to body temperature and increases by 5–7% per Celsius degree (approximately 3% per Fahrenheit degree). Hyperthermia should be avoided in all patients and cooling techniques should be considered if this is noted. Hypothermia reduces the cerebral metabolic rate and decreases the CBF by approximately 5% per degree of reduction in body temperature. Although this may be advantageous to the injured brain, it also increases the risk of cardiac abnormalities. Temperature instability in the brain-injured patient may be a grave prognostic sign. (Further information is available in Chapter 2.)

Once the patient is stable, radiographs of the chest and abdomen are recommended to evaluate for pulmonary contusions, pneumothorax and abdominal injuries. Pulmonary contusions are common following trauma and may not be at their most severe until 24 hours later. The abdomen should be evaluated through radiography and ultrasonography for the presence of free fluid, blood or urine, which may require additional therapy. Radiographs of the cervical vertebrae should also be considered, as head trauma can often be accompanied by fractures and luxations of these bones.

A delayed onset of scleral haemorrhage (12–24 hours) has been noted in dogs with head trauma. This usually resolves in 7–10 days, but the presence of subarachnoid haemorrhage should be strongly suspected.

In the days and weeks following head trauma, a few patients may develop endocrine disease related to hypothalamic/pituitary damage. Signs can be related to hypoadrenocorticism and inappropriate antidiuretic hormone secretion. (Further details on the detection and management of these conditions can be found in Chapter 3.)

Table 82 **Monitoring parameters for the cat and dog following head trauma**

MONITORING PARAMETER	SUGGESTED GOAL	SUGGESTED TREATMENT
Neurological examination	MGCS >15	• Ensure head elevation (30°) • Ensure all points below are addressed • Consider mannitol (see below) • Consider surgery (see text)
Blood pressure	MAP 80–120 mmHg	• Adjust fluid therapy • Pressor support (dopamine, 2–10 µg/kg/minute)
Blood gases	PaO_2 ≥90 mmHg $PaCO_2$ between 35 and 40 mmHg	• Oxygen supplementation • Consider active ventilation
Pulse oximetry (SpO_2)	SpO_2 ≥95%	• Oxygen supplementation • Consider active ventilation
Heart rate and rhythm	Avoid tachy- and bradycardias; avoid arrhythmias	• Adjust fluid therapy • Treat for pain • Address ICP • Treat arrhythmias specifically
Central venous pressure	5–12 cm H_2O	• Adjust fluid therapy
Respiratory rate and rhythm	10–25/minute	• Ventilate if necessary
Body temperature	37–38.5°C (98.6–101.3°F)	• Passive warming or cooling • NSAIDs if hyperthermic
Electrolytes	(See individual laboratory normal values)	• Adjust fluid therapy
Blood glucose	4–6 mmol/l (72–108 mg/dl)	• Adjust fluid therapy • Consider dextrose administration
Intracranial pressure	5–12 mmHg	• As for MGCS abnormalities

MGCS = Modified Glasgow Coma Scale.

Neurological assessment

A neurological assessment should be undertaken on any animal that has experienced a trauma. Assessment of neurological status in a patient after head trauma should initially be performed every 30–60 minutes. Frequent assessment allows for monitoring efficacy of treatment and early recognition of deterioration. Primarily, neurological evaluation of the patient serves to determine whether there are neurological deficits suggesting structural neurological lesions, where the lesions are located (i.e. at least intracranial, spinal and peripheral nerve) and the severity of the lesion(s). Detection of a spinal and/or peripheral nerve (e.g. brachial plexus) lesion can affect the prognosis of any patient with head trauma. Without any extracranial lesions, the prognosis associated with head trauma is dependent on the location and severity of the parenchymal lesions.

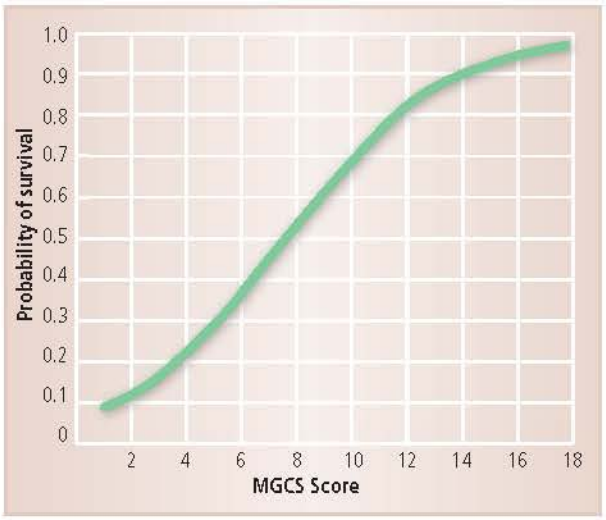
The assessment should include evaluation of state of consciousness, motor function and reflexes, pupil size and responsiveness, position and movement of the eyes and breathing pattern. The evaluation of pupil and eye function is the most accurate manner in which brainstem function can be assessed, and this is the most important part of the examination prognostically. A scoring system has been developed in veterinary patients to provide an objective assessment and allow for rational diagnostic and treatment decisions.

Modified Glasgow Coma Scale

The Glasgow Coma Scale is used in human medicine to assess head trauma patients by evaluating eye, verbal and motor responses. This scale has been modified and applied to veterinary patients. The Modified Glasgow Coma Scale (MGCS) evaluates motor activity, brainstem reflexes and the level of consciousness in veterinary patients, thus enabling initial and serial monitoring following injury. The three categories evaluated using the MGCS provide objective standards for scoring a patient between 1 and 6, with lower scores assigned to more severe clinical signs (*Table 83*). The scores from each category are added together to determine a patient's coma score, ranging from 3 to 18, and may be used to guide treatment decisions and prognosis (**288**).

Table 83 **Modified Glasgow Coma Scale**

	SCORE
Motor activity	
Normal gait, normal spinal reflexes	6
Hemiparesis, tetraparesis or decerebrate activity	5
Recumbent, intermittent extensor rigidity	4
Recumbent, constant extensor rigidity	3
Recumbent, constant extensor rigidity with opisthotonus	2
Recumbent, hypotonia of muscles, depressed or absent spinal reflexes	1
Brainstem reflexes	
Normal pupillary light reflexes and oculocephalic reflexes	6
Slow pupillary light reflexes and normal to reduced oculocephalic reflexes	5
Bilateral unresponsive miosis with normal to reduced oculocephalic reflexes	4
Pinpoint pupils with reduced to absent oculocephalic reflexes	3
Unilateral, unresponsive mydriasis with reduced to absent oculocephalic reflexes	2
Bilateral, unresponsive mydriasis with reduced to absent oculocephalic reflexes	1
Level of consciousness	
Occasional periods of alertness and responsive to environment	6
Depression or delirium, capable of responding but response may be inappropriate	5
Semicomatose, responsive to visual stimuli	4
Semicomatose, responsive to auditory stimuli	3
Semicomatose, responsive only to repeated noxious stimuli	2
Comatose, unresponsive to repeated noxious stimuli	1



◀ **288** The Modified Glasgow Coma Scale score is determined from the neurological examination. The score given can be anywhere between 3 and 18, with the lowest score representing the worst neurological situation. The score is almost linearly related to prognosis in terms of the probability of survival in the first 72 hours.

▼ **289** (a) Decerebrate rigidity seen in this 3-year-old Domestic Short hair cat is associated with coma, extensor rigidity in all four limbs and, occasionally, opisthotonus. This posture reflects a lesion of the midbrain.
(b) Decerebellate rigidity, which is often associated with normal consciousness, hyperextension of the forelimbs and spastic flexion of the hips, is seen here. This posture reflects a lesion of the rostral part of the cerebellum.

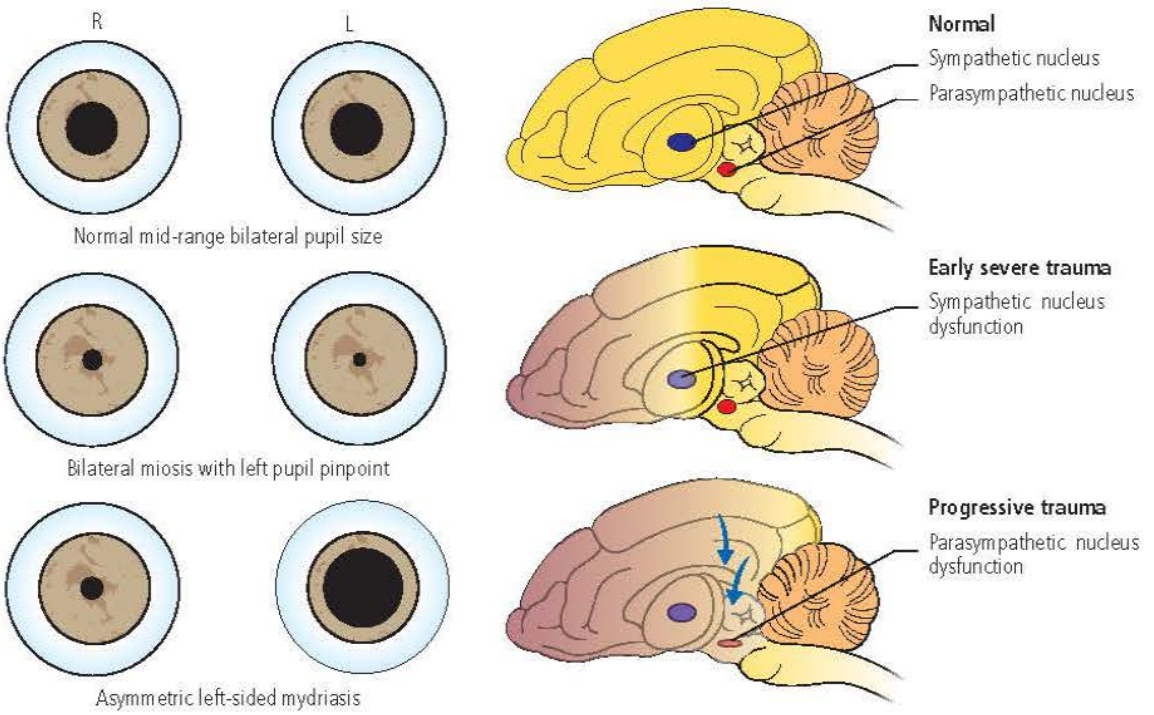
Assessment of limb function

The first category of the MGCS describes motor activity, limb tone and posture. Voluntary motor activity is characterized as normal, paretic or recumbent. Patients typically maintain some degree of voluntary motor activity even in altered states of consciousness unless they are comatose. Abnormal motor function usually reflects either brainstem injury or spinal cord injury; the latter may complicate the assessment of head trauma.

Tone is evaluated by placing the limbs through a passive range of motion. Increased tone can be seen following cranial trauma, as CNS inhibitory modulation to the LMNs is lost. However, severe brain injury leading to coma will be associated with decreased tone in all limbs. Spinal reflexes are tested primarily to assess nerve function, but may provide some information on cerebral activity. Animals may have exaggerated reflexes following cerebral injury and absent reflexes when comatose.

An animal's posture can also provide information about the location and degree of brain injury following trauma. Decerebrate rigidity (**289a**) can occur following cerebral trauma and suggests severe brain injury and a poor prognosis, as this posture reflects loss of communication between the cerebrum and the brainstem. Animals with decerebrate rigidity have opisthotonus with hyperextension of all four limbs and are stuporous or comatose, with abnormal pupillary light reactions. Decerebellate rigidity suggests acute cerebellar damage and may cause either flexion or extension of the hindlimbs (**289b**); however, consciousness may be normal.





▲ 290 **Pupil size following head trauma can progress from normal and reactive to light through miotic and pinpoint to dilated and unresponsive as the pathology progresses. The onset of miosis is related to brain injury causing damage to the sympathetic system responsible for pupil dilation. As the injury progresses and causes transtentorial herniation, the oculomotor nucleus becomes affected and results in pupil dilation.**

Assessment of brainstem reflexes

Pupil size, the PLR and the oculocephalic reflex should be immediately evaluated in all head trauma patients. Pupil size, symmetry and reactivity can provide valuable information about severity of brain injury and the prognosis. These parameters should be assessed frequently, as they can signal a deteriorating neurological status. Response of the pupils to a bright light indicates sufficient function of the retina, optic nerves, optic chiasm and rostral brainstem. The presence of miosis may indicate a lesion in the diencephalon, as the sympathetic innervation to the eye originates in the hypothalamus. The peripheral sympathetic innervation to the eye can also be affected by injury anywhere along its pathway through the brachial plexus, cranial mediastinum, cervical soft tissues and tympanic bulla, which often causes concurrent third eyelid elevation, enophthalmos and ptosis as part of Horner's syndrome. A miotic pupil may also be seen with ocular injury and spasm of the ciliary muscles of the iris; therefore, an ocular cause of miosis should be investigated.

Bilateral mydriasis that is unresponsive to light can indicate permanent midbrain damage or brain herniation and a poor prognosis. Other causes of mydriasis include decreased cerebral perfusion, postictal changes, trauma to the iris or retina, periorbital trauma or haematoma and previous ocular abnormalities.

Progression from miosis to mydriasis indicates a deteriorating neurological status and is an indication for immediate, aggressive therapy. Unilateral changes in pupil size may be seen early in deterioration. Paralysis of CN III can lead to mydriasis, loss of direct PLR, ptosis and ventrolateral strabismus. The CN III nucleus is located in the midbrain, therefore damage to this nucleus can be seen as a result of midbrain injury or compression secondary to transtentorial herniation (**290**).

The oculocephalic reflex (physiological nystagmus) is tested by moving the animal's head in vertical and horizontal planes to assess brainstem function and function of the CN nuclei innervating the extraocular eye muscles. If the animal's head cannot be moved without risk, a visual stimulus such as food or the owner should be moved or move around the animal. Absence of the oculocephalic reflex reflects injury to the brainstem. This reflex may also be delayed with cerebral injuries.

Assessment of consciousness

A patient's level of consciousness provides information regarding function of the cerebral cortex and the ARAS of the brainstem (see Chapter 6). Consciousness can be described as normal, depressed or obtunded, stuporous or comatose. An animal in a stupor is partially or completely unconscious, but will respond to noxious stimuli. A patient in a coma is unconscious and cannot be roused with noxious stimuli. Coma typically indicates severe cerebral injury or brainstem damage, which carries a guarded prognosis. These terms describe different levels or 'quantities' of consciousness and provide information regarding the degree of cerebral impairment. The quality of consciousness may be more difficult to evaluate objectively. Inappropriate activity suggesting confused or exaggerated responses to routine stimuli often confirms prosencephalon damage. It is important to note that the patient's BP, oxygenation status and temperature may all affect the animal's level of consciousness and so the latter should be re-evaluated after correction of the former vital parameters.

After evaluation, a patient should be assigned a score for each category to determine their overall coma score. This score can be used to monitor for improvement or deterioration of neurological status, guide diagnosis and treatment decisions (see below) and provide information about prognosis (see **288**).

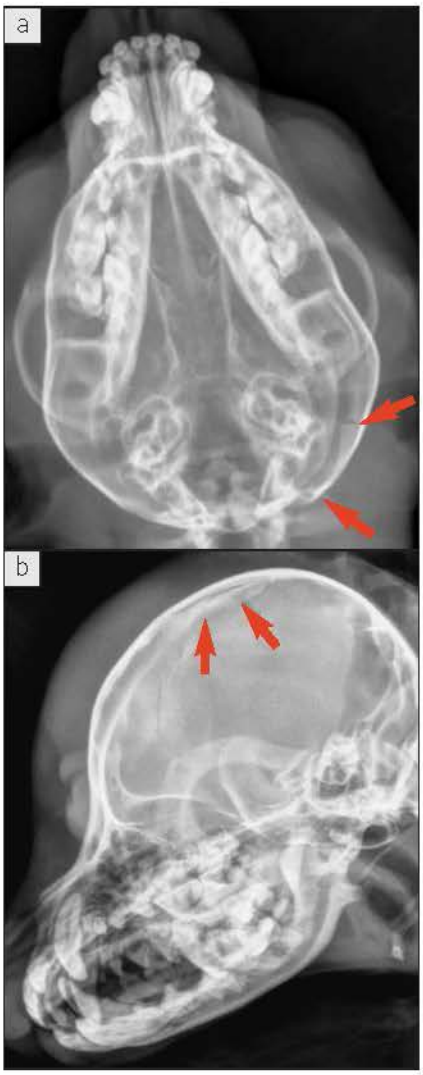
Assessment of respiration

Although assessment of respiratory patterns does not form part of the MGCS, intracranial trauma may lead to abnormal respiratory patterns and these should be assessed. Their associations with specific lesion localizations have not been confirmed in veterinary patients and so much of what we suspect is taken from the human literature. Hyperventilation may occur as a result of central mediation secondary to cerebral acidosis, cerebral hypoxia, mesencephalic injury or transtentorial herniation. A period of hyperventilation followed by apnoea is referred to as Cheyne–Stokes respiration, which is usually secondary to diencephalic injury and reduced responsiveness to partial pressure of arterial carbon dioxide. Respiration may also be classified as ataxic, which is indicative of severe brainstem damage and carries a grave prognosis. This breathing pattern is characterized by an irregular rate, rhythm and depth of respiration and is frequently accompanied by the Cushing reflex (i.e. hypertension and bradycardia), forming the Cushing triad.

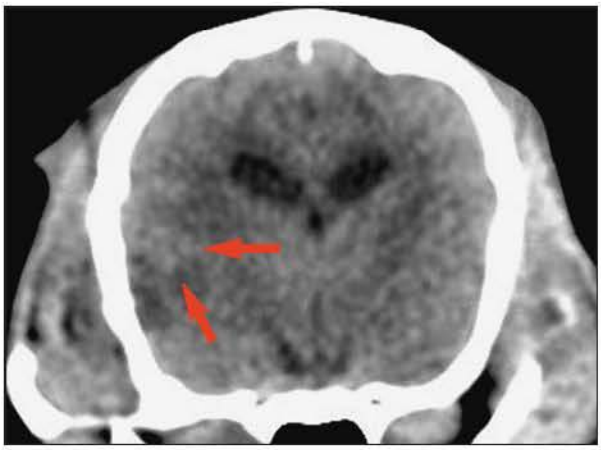
DIAGNOSIS

A diagnosis of head trauma is based primarily on a compatible history and clinical signs of intracranial neurological dysfunction. However, additional tests can be used to confirm the location and the extent of the injury. Advanced imaging of the brain (CT and MRI) should be reserved for patients who do not respond to initial treatment or for patients who deteriorate despite aggressive therapy. Both of these imaging modalities require anaesthesia, which can destabilize the head trauma patient unless the patient is in a coma on presentation.

Significant injury to the brain, leading to neurological signs, can occur without causing skull fractures or haematoma formation. Advanced imaging of the brain may be performed to evaluate for fractures, haemorrhage or parenchymal lesions; however, changes may not be seen even in a patient with severe neurological deficits.



▲ 291 (a) Dorsoventral skull radiograph of a 3-year-old Chihuahua that had been attacked by another dog. A linear fracture of the temporal bone is evident (arrows). (b) Lateral radiograph of a 2-year-old Chihuahua that was also attacked by another dog. There are comminuted fractures of the parietal bone (arrows), which could be depressed, but two views would be necessary and, possibly, advanced imaging to make an accurate assessment of injury. The dog was positioned carefully with flexion of the cervical spine in order to evaluate for the potential of vertebral abnormalities such as atlantoaxial subluxations, which were not present.



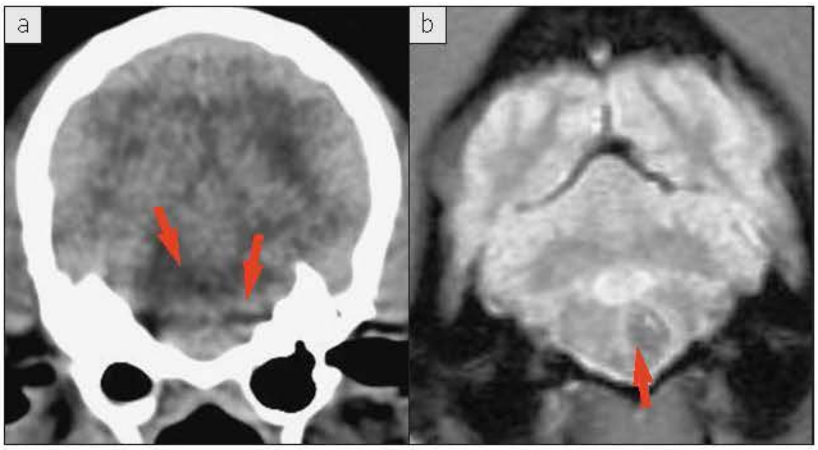
▲ 292 Transverse CT scan (soft tissue window) of a 7-year-old mixed breed dog 8 days after a head trauma. There is a large hypoattenuating lesion (arrows) in the temporal lobe, which was found to be a cystic lesion secondary to haemorrhage on postmortem examination.

Radiography

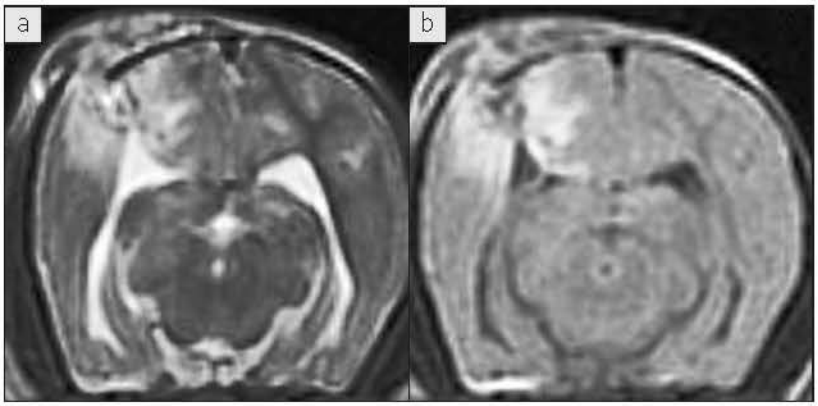
Skull radiography may reveal calvarial fractures, but provides no information regarding the brain parenchyma (**291**). Radiographs of the skull require anaesthesia for accurate positioning, which may be contraindicated in the acutely injured patient, and they can be difficult to interpret due to the irregularity of the skull bones. Radiography should not be limited to the skull following head trauma. Radiographs of the vertebral column, thorax and abdomen are indicated to evaluate for evidence of other injuries.

Ultrasonography

Ultrasonography can be used to evaluate the brain parenchyma crudely through a bony defect. Haemorrhage within the brain is hypoechoic in the acute stages, but may become hyperechoic over time. Doppler ultrasonography may be used to detect blood flow and indirectly assess ICP by evaluating the basilar artery.



◀ **293** (a) Transverse CT scan at the level of the caudal fossa demonstrates a beam-hardening artefact (arrows), due to the dense bone surrounding the parenchyma. This artefact interferes with lesion assessment in the brainstem. (b) Transverse T2*-weighted (gradient-echo) MR image at the level of the caudal fossa. This allows identification of a parenchymal lesion (arrow) secondary to trauma within the brainstem.



◀ **294** Transverse T2-weighted (a) and transverse T2-weighted FLAIR (b) MR images of a dog bite. The penetrating lesion can be identified on both images, but the hyperintensity on the FLAIR image more clearly indicates the surrounding oedema. FLAIR MRI is more sensitive to oedematous lesions as it can suppress signals from free water such as CSF.

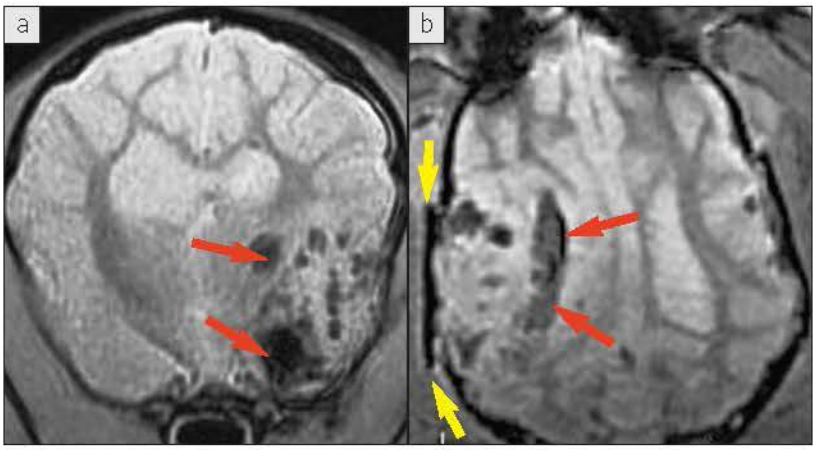
Computed tomography

CT allows superior evaluation of bony structures and is preferred over conventional radiography, especially considering the 3D reconstruction capabilities. In addition, CT can be used to diagnose intracranial haemorrhage, alterations in ventricular size or shape, midline shift of the falx cerebri and oedema. CT does not provide good soft tissue detail of the brain parenchyma, but is frequently the preferred modality for evaluation of human head trauma patients for surgical intervention because of the speed of image acquisition. Typically, haemorrhage is hyperattenuating (hyperdense) on a CT scan in the acute stages. Over time, the density decreases with clot resorption, creating a hypoattenuating lesion similar to oedema (**292**). CT can provide images for surgical planning, but should only be pursued in patients who are severely affected or are deteriorating and require surgical intervention.

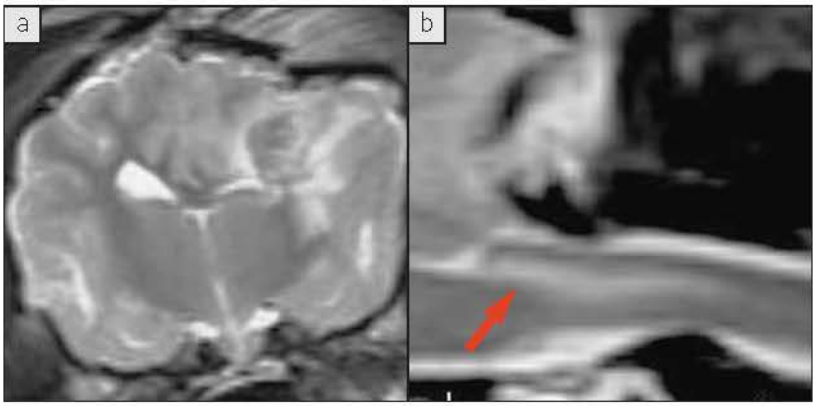
Magnetic resonance imaging

MRI allows superior soft tissue detail and is preferred for evaluation of the brain, especially the caudal fossa, which does not image well with CT (**293**). MRI can detect more subtle parenchymal changes that may be missed on CT and may provide information about the prognosis. Haematomas or haemorrhage, parenchymal contusions and oedema are readily apparent on MR images (**294**; **295**, next page). Although CT is preferred for evaluation of bony structures, fractures can also be identified on MRI (**296**, next page), most proficiently using STIR and gradient echo sequences (see Chapter 4 for further details).

Typically, CT and MRI are only pursued in patients who fail to respond to aggressive medical therapy or patients who deteriorate and may require surgical intervention. MRI findings were recently correlated with prognosis in veterinary head trauma patients, therefore its use may be of specific additional benefit (see below).



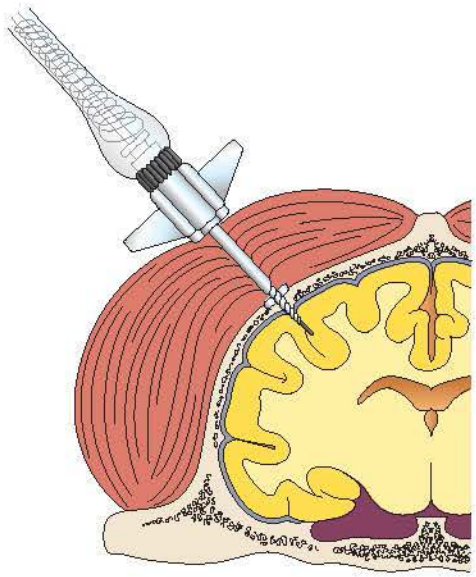
◀ 295 Transverse (a) and dorsal T2*-weighted (gradient-echo) (b) MR images of a Jack Russell Terrier following a head trauma. The hypointense (signal void) or black areas within the parenchyma (red arrows) are compatible with haemorrhage. The dorsal image (b) also reveals a linear skull fracture (yellow arrows), which can be best seen on T2* images.



◀ 296 (a) Transverse T2-weighted MR image of a Labrador Retriever revealing a comminuted depressed fracture of the frontal bone. (b) Sagittal T2*-weighted (gradient-echo) MR image of a Corgi revealing a depressed occipital bone fracture, as well as hyperintensity within the cranial cervical spinal cord (arrow), compatible with oedema secondary to the compressive fracture.

Intracranial pressure monitoring

ICP may be monitored through placement of a pressure transducer or fibre-optic transducer into the epidural, intra-axial or intraventricular space (**297**). ICP monitoring is frequently pursued in human head trauma patients, but it may have limitations in veterinary patients. ICP monitoring is not without risk and may lead to the development of oedema, haemorrhage, parenchymal damage and infection.



▶ 297 An intracranial pressure (ICP) monitor often relies on a fibre-optic transducer placed within the cerebral parenchyma to record fluctuations in ICP.

MANAGEMENT

Treatment strategies should be directed towards both systemic and neurological stabilization in an effort to minimize secondary damage. Several aspects of treatment exist. Systemic stabilization involves correction of systemic shock and respiratory abnormalities with fluid therapy and oxygen therapy/management of ventilation, respectively. The second aspect of treatment involves measures to reduce elevations in ICP and cerebral metabolic rate. Finally, some animals require surgical intervention because of lack of improvement or a declining neurological status.

Corticosteroids are no longer recommended in head trauma patients. Their use has been extensively evaluated in people, which has shown no beneficial effect and may even result in worse morbidity and mortality rates. Detrimental effects of corticosteroids include immunosuppression, hyperglycaemia and gastrointestinal disturbances.

Treatment of head trauma is proposed in a progressive, tiered system, based on the severity of injury and the success of the initial therapy (**298**, next page). Tier 1 treatments are administered to all patients; Tier 2 treatments are administered to all patients with an MGCS of <8 and failure of Tier 1 treatments; Tier 3 treatments are administered to all patients with an MGCS of <8 and failure of Tier 2 treatments.

Tier 1 therapy

Fluid therapy

The goal of fluid therapy in the head trauma patient is to restore a normovolaemic state. It is deleterious to dehydrate an animal in an attempt to reduce cerebral oedema. Aggressive fluid therapy and systemic monitoring are required to ensure normovolaemia and so maintain adequate CPP. Detailed descriptions of fluid therapy indications and techniques are provided in Chapter 31.

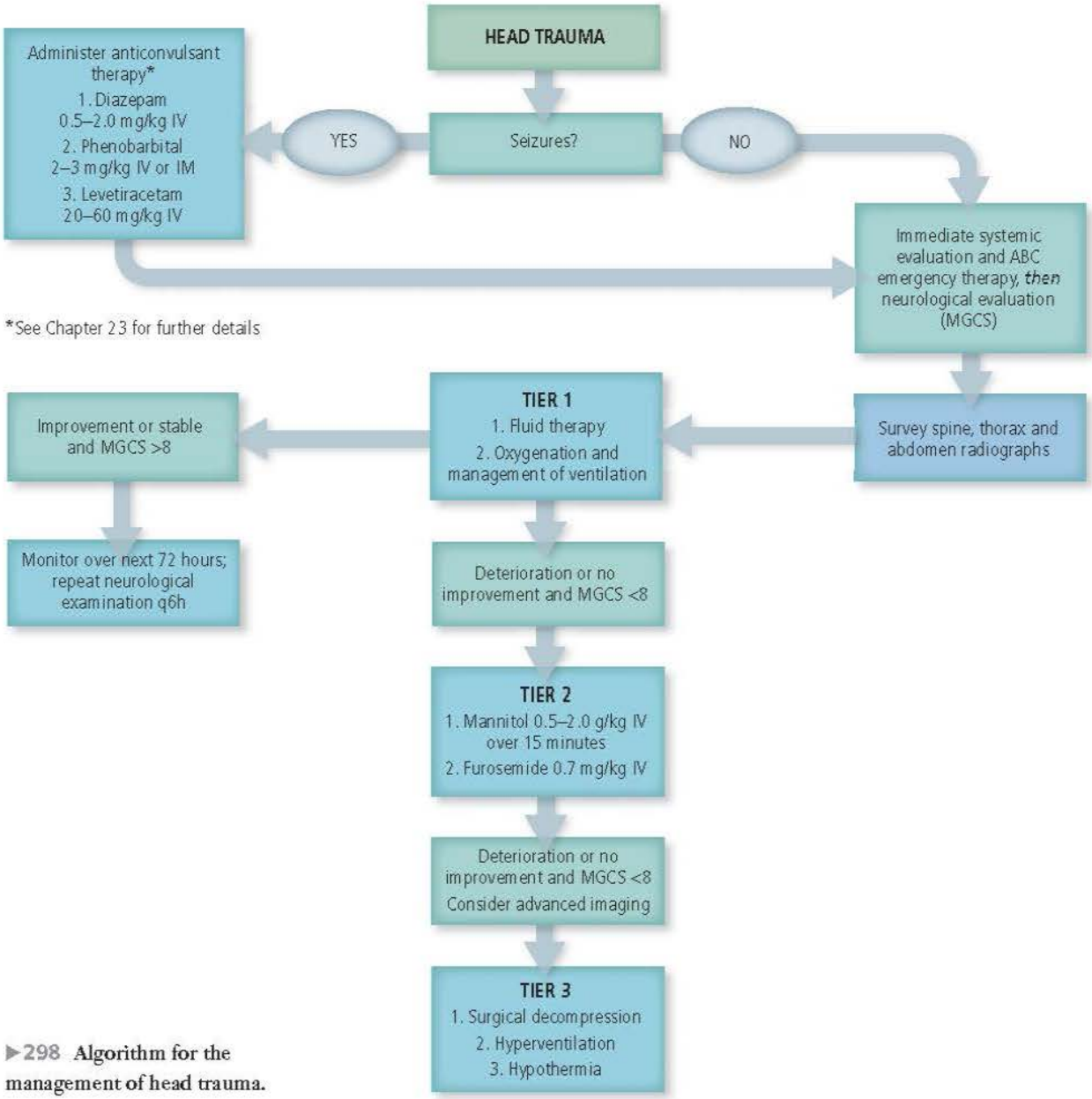
Crystalloid, hypertonic and colloid fluids should be given concurrently to help restore and maintain blood volume following trauma. Crystalloids are usually given initially for the treatment of systemic shock. These balanced electrolyte solutions may be given at shock doses (90 ml/kg for dogs; 60 ml/kg for cats). Typically, it is recommended that the shock dose be given in fractions starting with one-third to one-fourth of the calculated volume, frequently reassessing the patient for normalization of MABP, mentation and CVP if monitored, and giving additional fractions if needed. Unfortunately, crystalloid solutions will extravasate into the interstitium within 1 hour of administration, thus requiring additional fluid resuscitation.

Hypertonic and colloid fluid therapy can rapidly restore blood volume using low-volume fluid resuscitation; in addition, colloids remain in the vasculature longer than crystalloid fluids. These fluids should be used with caution as without concurrent administration of crystalloid solutions, hypertonic and colloid solutions can lead to dehydration. Other benefits of hypertonic fluids include the ability to improve cardiac output, restore normovolaemia and reduce inflammation after trauma. Hypertonic saline may be preferred in hypovolaemic, hypotensive patients with increased ICP.

Hypertonic saline improves CPP and blood flow by rapidly restoring intravascular blood volume. Also, the high sodium content of hypertonic saline draws fluid from the interstitial and intracellular spaces, subsequently reducing ICP. Contraindications to administration of hypertonic saline include systemic dehydration and hypernatraemia. Hypertonic saline only remains within the vasculature for about 1 hour, therefore it should be followed by colloids to maximize its effects. A dose of 5–6 ml/kg (dogs) and 2–4 ml/kg (cats) of 7.5% NaCl should be given over 5–10 minutes.

Colloids (e.g. Hetastarch, Dextran-70) allow for low-volume fluid resuscitation, especially if total protein concentrations are below 50 g/l (5 g/dl). These fluids also draw fluid from the interstitial and intracellular spaces, but have the added benefit of staying within the intravascular space longer than crystalloids. Hetastarch is typically given as 5–6 ml/kg boluses in dogs and 2–4 ml/kg in cats over 5–10 minutes, with frequent patient re-evaluation. A total dose of 20 ml/kg/day may be given. In addition to volume resuscitation, oxygen carrying capacity should be considered, especially if the PCV is <0.3 l/l (<30%). Further information on blood transfusions and the use of oxyglobin can be found in Chapter 31. The use of oxyglobin and other haemoglobin-based oxygen carriers has not been well evaluated in head trauma, but initial studies suggest that they could play a valuable role.

Systemic BP may require management to maintain adequate CPP. An MAP of 80–100 mmHg should be the target BP. Hypotension should initially be treated with fluid resuscitation, but if persistent may need treatment



▶298 **Algorithm for the management of head trauma.**

with vasoactive agents (e.g. dopamine, 2–10 g/kg/minute). Systemic hypertension may occur as a sequela to intracranial hypertension as a result of the Cushing reflex. Raised ICP leading to systemic hypertension should be treated aggressively. The use of additional drugs to modulate the BP should be avoided unless all attempts to lower ICP have been exhausted.

Head trauma patients should be positioned to maximize arterial circulation to the brain and improve venous drainage. This goal is best achieved by elevating the animal's head at a 30° angle. It is important to ensure that the jugular veins are not occluded and that no restrictive collars are placed around the neck, which would elevate ICP.

Oxygen therapy and management of ventilation

Oxygen supplementation is recommended in all patients following head trauma. Control of PaO_2 and $PaCO_2$ is mandatory and will affect both cerebral haemodynamics and ICP. Permissive hypercapnea should be avoided because of its cerebral vasodilatory effect, which increases ICP. Hypocapnea can produce cerebral vasoconstriction through serum and CSF alkalosis. Reduction in CBF and ICP is almost immediate, although peak ICP reduction may take up to 30 minutes after $PaCO_2$ has been changed.

The amount of oxygen within the blood (SpO_2) can be assessed with a pulse oximeter, measuring the PaO_2 with blood gas analysis in conjunction with measurement of circulating haemoglobin concentration. Calculation of oxygen delivery to the tissues requires measurement of both arterial oxygen content and cardiac output. Measurement of mixed venous oxygen can provide an indirect measure of adequacy of oxygen supply to the tissues. The amount of CO_2 within the blood can also be assessed by arterial blood gas analysis, as well as via capnography. Capnography provides breath by breath assessment of the adequacy of ventilation assuming normal cardiovascular function. This technique measures CO_2 in the expired patient gases ($P'ETCO_2$), which approximates to the CO_2 tension in the alveoli. As alveolar gases should be in equilibrium with arterial blood, $P'ETCO_2$ can be used to approximate $PaCO_2$ unless severe pulmonary dysfunction is present.

The goal of oxygen therapy and management of ventilation is to maintain PaO_2 greater than or equal to 90 mmHg and $PaCO_2$ between 35 and 40mmHg. If the patient is able to ventilate spontaneously and effectively, supplemental oxygen should be delivered via 'flow-by'; confinement within an oxygen cage prevents frequent monitoring. Face masks and nasal catheters should be avoided if possible as they can cause anxiety, which may contribute to elevation in ICP.

Patients with severe head injury require mechanical ventilation to maintain these arterial blood gas concentrations at their optimal levels. The absolute indications for mechanical ventilation include loss of consciousness, a rising $PaCO_2$ of >50 mmHg and falling SpO_2 despite appropriate treatment.

There are no contraindications to the use of PEEP in hypoxaemic patients. With adequate volume resuscitation, PEEP does not increase ICP nor does it lower CPP, and it may actually decrease ICP as a result of improved cerebral oxygenation. Assessment of adequacy of ventilation can be made by measurement of arterial CO_2 or, alternatively, by using capnography. Details on capnography and blood gas analysis, as well as details on the indications and techniques associated with ventilating patients, can be found in Chapter 2.

Tier 2 therapy

Diuretics

ICP can be addressed aggressively with the administration of osmotic diuretics (e.g. mannitol); however, they should not be given to any patient without being certain that the patient has been volume resuscitated. If not, their use can precipitate acute renal failure. For this reason they are reserved as Tier 2 therapies.

Mannitol improves CBF and reduces ICP by decreasing oedema. After administration, mannitol expands the plasma volume and reduces blood viscosity, which improves CBF and delivery of oxygen to the brain. In addition, mannitol assists in scavenging free radicals, which contribute to secondary injury processes. Vasoconstriction occurs as a sequela to the increased partial pressure of oxygen, leading to an immediate decrease in ICP. Also, the osmotic effect of mannitol reduces extracellular fluid volume within the brain.

Mannitol (0.5–2.0 g/kg) should be given as a bolus over 15 minutes to optimize the plasma expanding effect. Continuous infusions of mannitol increase the permeability of the blood–brain barrier, exacerbating oedema. Lower doses of mannitol are as effective at decreasing ICP as higher doses, but may not last as long. Mannitol reduces brain oedema over about 15–30 minutes after administration and has an effect for approximately 2–5 hours. Repeated dosing with mannitol can cause diuresis, leading to reduced plasma volume, increased osmolarity, intracellular dehydration, hypotension and ischaemia. Therefore, adequate isotonic crystalloid and colloid therapy is critical to maintain hydration. Administration of mannitol should be reserved for critical patients (MGCS of <8), a deteriorating patient or a patient failing

to respond to other treatment. Administration of furosemide (0.7 mg/kg) prior to administration of mannitol may have a synergistic effect at lowering ICP. Currently, there is no evidence to support the view that mannitol is contraindicated in the presence of intracranial haemorrhage, as has been suggested.

Seizure therapy

Seizures should be treated aggressively to prevent worsening of the secondary effects in the brain parenchyma due to associated brain hypoxia and subsequent development of oedema. Seizure activity may occur immediately following trauma or may be delayed in onset. The need for antiseizure prophylaxis after severe brain trauma remains controversial in human medicine. Human patients treated in the first 7 days after head trauma with anticonvulsants have a significantly lower risk of post-traumatic seizures within this time period than if not treated. Beyond 7 days from injury there appears to be no benefit to prophylactic treatment.

Diazepam (0.5–2.0 mg/kg) can be given intravenously to treat seizures. Phenobarbital (2–3 mg/kg IV or IM) may also be given and continued parenterally, following a loading dose (18–24 mg/kg IV over a 24–48 hour period), if necessary. Recently, the use of intravenous levetiracetam (20–60 mg/kg) has been described for emergency seizure treatment, as it may be effective for up to 8 hours without needing hepatic metabolism. Refractory seizures at the time of head trauma may require additional therapy such as a continuous infusion of diazepam (0.5–1.0 mg/kg/hour) or propofol (4–8 mg/kg bolus to effect followed by 1–5 mg/kg/hour CRI). Emergncy seizure treatment is discussed in greater detail in Chaper 23.

Some patients may require long-term management of seizure activity with antiepileptic medications. However, if maintenance therapy is continued beyond 7 days and seizure activity is not noted over a 3–6 month period, antiepileptic treatment may be slowly withdrawn. Therapy should be reinstituted if seizures return with an unacceptable frequency.

Tier 3 therapy

Failure of fluid therapy, oxygenation and ventilation strategies and osmotic diuretics to stabilize the patient and/or improve the neurological status significantly warrants radical therapy and such cases should be considered for advanced imaging such as MRI. The treatments discussed below have not been evaluated in veterinary medicine in terms of their efficacy and they remain controversial or unproven in human head trauma.

Hyperventilation

Hyperventilation has been suggested as a method of lowering ICP quickly. Hypercapnea causes vasodilation and subsequent increases in ICP, therefore hypoventilation should be avoided. Mechanical or manual ventilation may be used to lower $PaCO_2$ (<35 mmHg) and reduce ICP in deteriorating patients responsive to no other treatment and with no surgical lesions. The prolonged use of hyperventilation should be avoided, as a reduction in cerebral $PaCO_2$ of less than 30–35 mmHg causes vasoconstriction, which ultimately leads to decreased CBF and ischaemia.

Hypothermia

At the time of writing, hypothermia is an experimental treatment that has not been validated in veterinary medicine and remains controversial in human medicine. Following trauma, the cerebral metabolic rate may be increased, leading to exacerbating secondary effects. Controlled hypothermia and induction of coma reduce the cerebral metabolic rate and have been reported in human head trauma patients and, recently, in a veterinary patient. Hypothermia can be achieved by cooling a patient to a rectal temperature of 32–35°C (89.6–95.0°F), which reduces cerebral metabolic rate and oxygen consumption and leads to decreased CBF and ICP. However, reduction of core body temperature carries risks and may lead to the development of cardiac arrhythmias, coagulopathies, electrolyte disturbances, hypovolaemia and insulin resistance. Coma may also be induced using barbiturates, but this prevents neurological evaluation and requires induction of mechanical ventilation.

Progesterone therapy

Progesterone therapy has been used experimentally in rats and humans to reduce cerebral oedema and for its neuroprotective effects. Systemic injections of progesterone decrease excitotoxicity by reducing the effects of glutamate and enhancing the effects of GABA. Administration of progesterone to rats following traumatic brain injury has been shown significantly to improve functional outcome following injury, decrease neuronal loss, reduce accumulation of astrocytes, reduce inflammation by blunting cytokine generation and improve vasogenic and cytotoxic oedema. Additionally, progesterone has antioxidant effects and reduces lipid peroxidation and oxidative stress by decreasing free radical generation and enhancing endogenous free radical systems.

Surgery

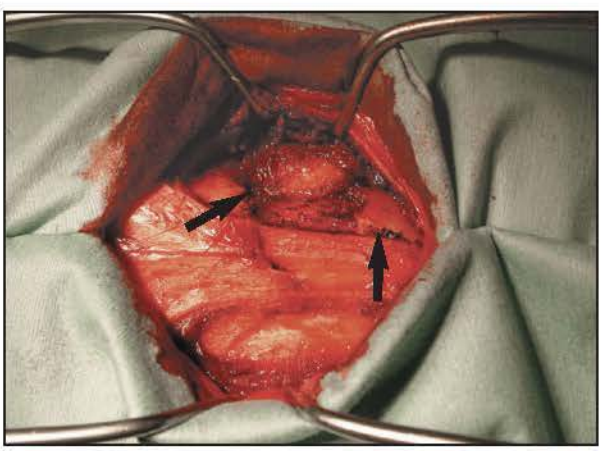
Surgical intervention is reserved for patients that do not improve or deteriorate despite aggressive medical therapy. Advanced imaging (CT or MRI) is necessary for surgical planning and is also used in medically refractory patients. Surgery may be indicated to remove haematomas, relieve ICP or address skull fractures. Ventricular obliteration and mass effect identified on advanced imaging should be considered strong indicators for surgical treatment in any animal that does not improve with medical therapy.

Extra-axial haematomas can be removed through a generous craniectomy. Surgery in these patients may lead to significant haemorrhage that requires blood transfusions. Removal of haematomas may exacerbate bleeding as compression of bleeding vessels is removed, leading to re-accumulation of blood even after surgery. Intra-axial haematomas are typically managed conservatively. Surgery may be indicated in a deteriorating patient with subacute enlargement of a previously small haematoma.

Haemorrhagic parenchymal contusions can cause severe neurological signs depending on their location. They are typically managed conservatively. Cerebellar contusions causing 4th ventricle and brainstem compression are an indication for surgery in humans in an effort to reduce continued compression and the risk of herniation. Surgery for cerebellar contusions may be indicated prior to neurological deterioration because these signs are less reversible with conservative management.

Intracranial hypertension should be treated initially with the therapies discussed previously. However, in about 20% of human head trauma patients, additional decompressive surgery is also required. Surgery is beneficial in deteriorating patients before irreversible brain damage, indicated by bilateral pupillary dilation, occurs. Surgical intervention for intracranial hypertension involves the creation of a large craniectomy over the most affected site, followed by a durectomy or duraplasty to allow the brain to swell.

Typically, skull fractures do not require surgical intervention. However, significantly contaminated, comminuted fractures may require surgical débridement, especially if open (**299**). In dogs, such fractures of the frontal sinus may be associated with traumatic pneumocephalus and this should be considered in any dog deteriorating despite aggressive medical therapy. If surgical intervention is pursued, aggressive débridement should include removal of all devitalized tissues and bone and should be guided by imaging. Large bone fragments may be spared and replaced after thorough débridement, cleaning and soaking in an antibiotic solution.



▲ **299** Intraoperative view of the dorsal calvarium of a 4-year-old Dachshund that was kicked by a horse. There are multiple linear fractures evident (arrows). Surgery was only necessary because the fractures were associated with extra-axial haemorrhage, which warranted removal due to the deteriorating neurological status.

Following surgery, seizure and antibiotic prophylaxis are recommended. Phenobarbital (2–3 mg/kg IV q6–8h for 48 hours, followed by maintenance parenteral therapy) is advised. An alternative approach is the use of levetiracetam (20–60 mg/kg IV q8h, followed by 20 mg/kg PO q8h).

General supportive care

Urinary catheters should be placed to provide proper bladder management in recumbent patients and to monitor urinary output. Adequate urine output is between 1 and 2 ml/kg/hour, but it should match the volume of fluid given to the patient. Reduced urine output could indicate continued dehydration, hypovolaemia or reduced renal function. Increased urine output may be seen secondary to osmotic diuretic therapy as well as central diabetes insipidus, which can occur as a sequela to intracranial trauma.

Adequate nutrition is critical to the recovery of patients following brain injury; however, hyperglycaemia should be avoided, as it increases the cerebral metabolic rate and promotes anaerobic metabolism, leading to cerebral acidosis. Initially, nutrition may be supplemented through naso-oesophageal feeding tubes. Placement may be contraindicated in patients with elevated ICP, as placement can stimulate sneezing, which causes transient increases in ICP. In patients with proper oesophageal function, oesophagostomy tubes allow medium- to long-term management of feeding. Gastrotomy tubes offer nutritional support in patients with poor oesophageal function and allow long-term nutritional support.

Recumbent patients require proper bedding and monitoring to prevent the development of decubital ulcers. Bedding should be well padded and evaluated frequently to maintain a clean and dry surface. Patients require alternation of recumbency every 4–6 hours and frequent evaluation of pressure points for development of decubital ulcers.

PROGNOSIS

The prognosis is dependent on the severity of neurological signs and the response to treatment. The association between a patient's score using the MGCS and prognosis has been evaluated. This showed an almost linear correlation between score and probability of survival within the first 72 hours (see **288**). Patients with high MGSC scores had a high probability of survival, while patients with low scores were unlikely to survive. A score of 8 on the MGSC was associated with about a 50% chance of survival. The MGCS has recently been evaluated with long-term survival at 1 and 6 months following injury. Again, a linear trend between MGCS and survival at 1 and 6 months was demonstrated. An association between the MGCS and long-term patient outcome could allow a prediction of acceptable patient recovery and aid in decision making at the time of injury.

In humans with head trauma, hyperglycaemia on admission is a frequent component of the stress response to the injury, a significant indicator of severity of injury and a potent predictor of the patient's outcome. A recent study in dogs and cats suggests that head trauma in these species may be associated with hyperglycaemia and that the degree of hyperglycaemia can be associated with the severity of the head trauma. However, the degree of hyperglycaemia does not seem to be associated with outcome for dogs and cats with head trauma. Because hyperglycaemia can potentiate neurological injury, iatrogenic hyperglycaemia should be avoided in patients with head trauma.

MRI evaluation of head trauma patients has also been assessed in conjunction with the MGCS to determine patient outcome. MRI changes were graded (I–IV) with increasing severity of injury and evaluated with patient outcome at 1 and 6 months following injury. Grade was significantly associated with patient outcome. A higher MRI grade correlated with reduced likelihood of survival. In addition, the presence of a midline shift on MRI was significantly associated with prognosis, with dogs without a midline shift more likely to survive to 1 month.

Severely affected animals can achieve a functional recovery with proper patient assessment and monitoring, appropriate aggressive treatment and time.

SPINAL TRAUMA

Natasha Olby

INTRODUCTION

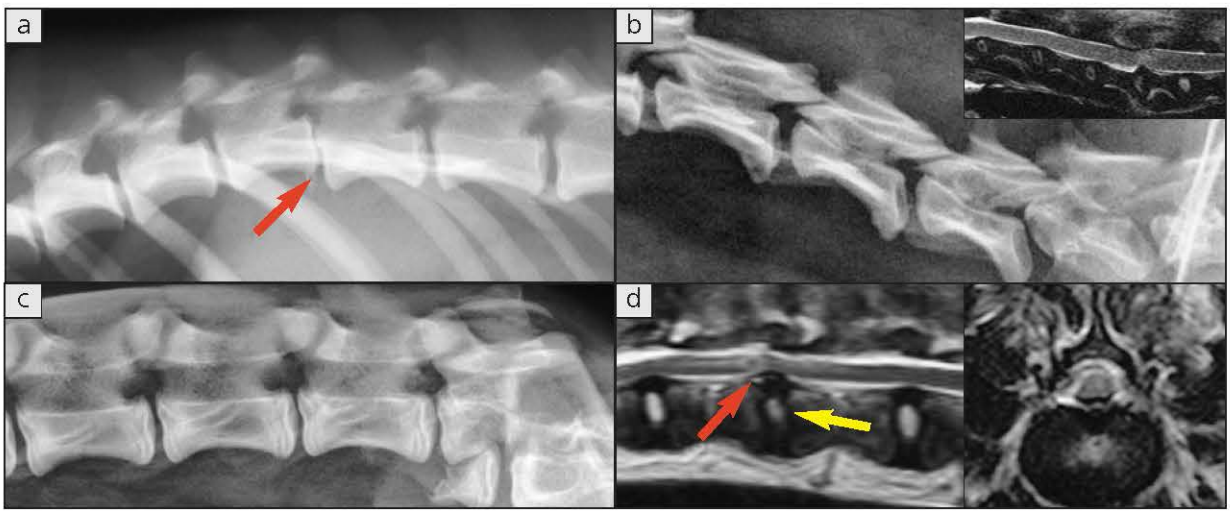
Spinal trauma implies external trauma to the vertebral column. The consequences include vertebral fractures, luxations and subluxations, acute disc herniations and soft tissue injuries. Spinal cord contusion, laceration and compression, and nerve root entrapment can all occur as a result of spinal trauma.

AETIOLOGY AND PATHOPHYSIOLOGY

The most common cause of spinal trauma is a road traffic accident. Other causes include falls, dog fights, gun shots, falling objects (e.g. trees) and accidental owner-induced injuries (especially cats and toy breeds of dog).

The clinical signs associated with spinal trauma are caused by injury to the spinal cord, the spinal nerves as they exit the vertebral canal and the vertebral column itself. The various injuries resulting from trauma include vertebral fractures, subluxations and luxations, flexion/extension injuries and traumatic disc herniations (**300**).

▼ 300 Various types of vertebral and spinal cord trauma. (a) Lateral radiograph of the thoracolumbar spine showing subluxation at T12/T13 (arrow) (caused by flexion and rotation of the spine). There is no evidence of a fracture. (b) Lateral radiograph of the cervical spine. The articular facets at C5/C6 have become luxated, causing a syndrome called 'locked facets' (caused by flexion and rotation of the spine). The inset is a sagittal T2-weighted MR image showing compression of the spinal cord at the site of the luxation. (c) Displaced vertebral body fracture of L7 (caused by flexion and rotation of the spine). (d) Sagittal and transverse T2-weighted MR images of the lumbar spine showing a traumatic disc herniation (caused by hyperflexion). There is a small amount of disc material in the canal (red arrow) and the affected nucleus (yellow arrow) is less hydrated than the adjacent nuclei.



Subluxation and luxation can occur in combination with a vertebral fracture or be due to soft tissue disruption only, without evidence of vertebral injury. These injuries occur most frequently at the lumbosacral, thoracolumbar and atlantoaxial junctions. Cats are more likely to suffer from sacrocaudal fractures than dogs and typically have a combination of fracture and luxation, whereas approximately 20% of dogs suffer a luxation only.

Several different types of vertebral fracture and luxation can occur dependent on the combination of loading forces applied and the location along the spine. Forces can be divided into axial loading, flexion and extension, and rotational, with each producing a different type of vertebral column injury. Combinations of these forces also produce characteristic injuries (*Table 84*). This type of classification can be useful in the development of a treatment plan when used in combination with information on the severity of spinal cord compression.

These events can cause spinal cord contusion and laceration and can result in compression by bone, soft tissue or blood (haematomas). Ongoing instability can result in repeated contusive injuries, additional laceration of the cord and increasing severity of compression.

Spinal cord contusion

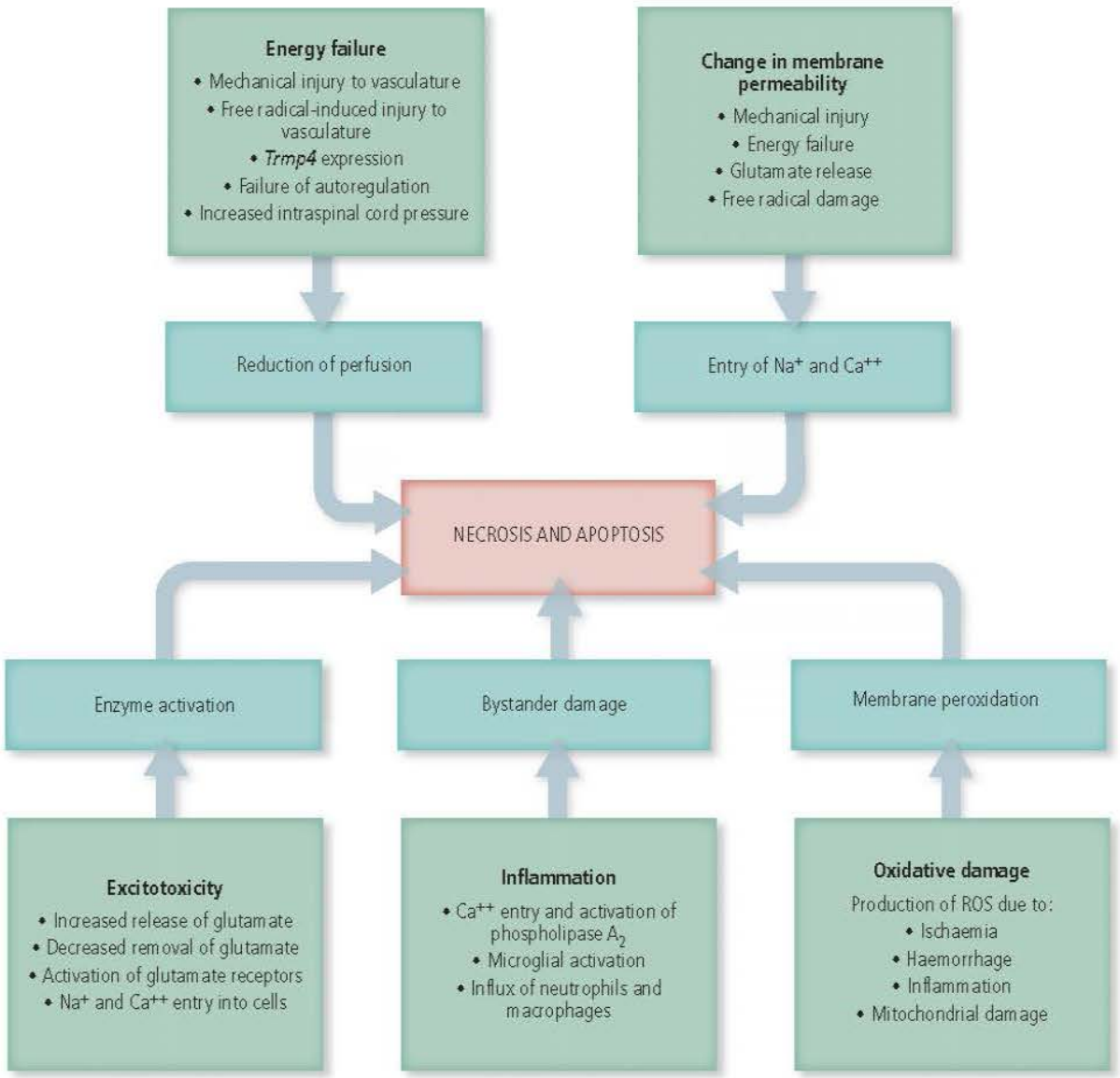
Contusive injury to the spinal cord causes primary mechanical injury to the parenchyma and vasculature, and secondary damage that is responsible for an expanding zone of necrosis and apoptosis. The majority of the secondary damage occurs in the 24–48 hour period after the initial injury, but ongoing apoptotic cell death can be detected months and even years later. Primary damage to the spinal cord can be devastating, resulting in transection of the spinal cord. Indeed, displaced vertebral fractures coupled with the clinical finding of paralysis and loss of nociception indicates an extremely poor prognosis for recovery of neurological function.

Secondary injury develops because of biochemical and metabolic events that interact to produce cell death. The mechanisms can be summarized as energy failure, changes in membrane permeability, excitotoxicity, oxidative damage and inflammation (**301**). Damage to the vasculature by the initial impact causes energy failure in neurons and glia, which in turn causes failure or reversal of ion pumps, loss of membrane polarization and entry of sodium and calcium into cells, producing cytotoxic oedema. Reactive oxygen species (ROS) (free radicals)

Table 84 **Loading forces in spinal trauma**

LOADING FORCE	VERTEBRAL COLUMN INJURY	THERAPEUTIC CONSIDERATIONS
Flexion	Traumatic disc herniation	May be stable May require decompression
Extension	Fracture of articular facets Fracture of dorsal lamina and spinous processes	May be stable May require decompression
Flexion and rotation	Luxation/subluxations (soft tissues of vertebral column disrupted) Fracture/luxations (vertebral body and articular facets fractured)	Typically unstable Realignment may provide adequate decompression Additional decompression may be necessary Significant spinal cord laceration may be present
Flexion and axial loading	Wedge compression fractures (vertebral body) Burst fractures	Variable stability May require decompression
Flexion, extension, rotation, axial loading	Transverse fracture	Often stable May require decompression

▼ 301 **Diagrammatic representation of the changes that occur following contusive injury to the spinal cord.**



produced as a result of haemorrhage, ischaemia and mitochrondrial failure cause damage to cell membranes and ongoing destruction of the microvascular bed, increasing the zone of ischaemia. Intraparenchymal haemorrhage has also been linked to a rapid increase in expression of *Trmp4*, a gene that encodes monovalent cation channels. Although the mechanism of this phenomenon is poorly understood, prevention of *Trmp4* expression results in reduced haemorrhage and improved outcome. Finally, local perfusion is reduced by increased intraspinal cord pressure due to cytotoxic oedema and haemorrhage and by a failure of autoregulatory mechanisms.

The importance of decreased perfusion in initiating and perpetuating secondary damage is clear. It is critical, therefore, to maintain BP and oxygenation within normal limits. Both hypotension and hypoxaemia can greatly exacerbate injury severity.

Membrane permeability is increased by the initial mechanical injury, thus exacerbating the imbalance of intra- and extracellular ions. In addition, extracellular concentrations of the excitotoxin glutamate (and, to a lesser extent, aspartate) are elevated. This results from neuronal release caused by the initial mechanical injury and energy failure, and by failure of astrocytic uptake. Activation of NMDA, alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and kainate receptors by glutamate increases sodium and calcium entry into neurons. Calcium entry causes cell death by activation of apoptosis-inducing proteases such as calpain and caspase, initiation of an inflammatory response by activation of phospholipase A_2 and further diminishing energy sources by binding intracellular phosphates.

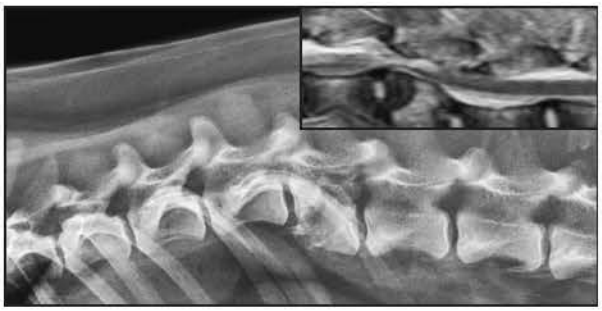
The inflammatory response has both beneficial and detrimental effects. Early production of thromboxane and prostaglandins by activation of phospholipase A_2 and microglial production of cytokines, such as interleukin-1 (IL-1) and tumour necrosis factor-alpha (TNF-α) initiate the inflammatory response. There is massive recruitment of neutrophils to the injured tissue within a few hours, followed by macrophage recruitment that peaks around 5 days after injury. Necrotic tissue is removed eventually, leaving a cystic cavity (syrinx). Activated phagocytic cells can release substances that are toxic to adjacent intact tissue, causing demyelination and axonal damage; a reduction in macrophage influx has been associated with an improved outcome. However, the inflammatory reaction plays an important role in tissue repair, revascularization and axonal sprouting.

Spinal cord compression

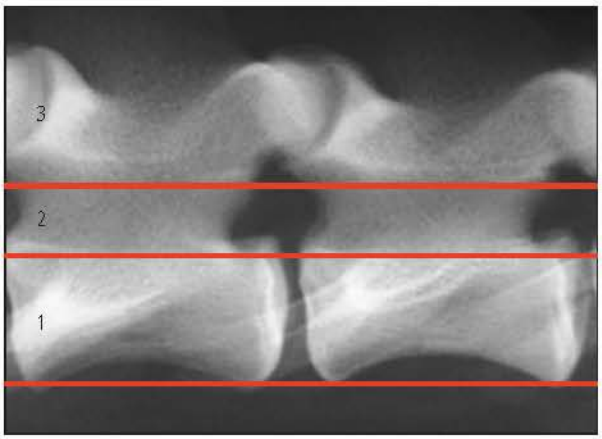
Compression of the spinal cord reduces perfusion, potentially causing neuronal and glial cell death by the secondary injury mechanisms described above. Demyelination is a common finding histopathologically, as a result of both direct damage to myelin and death of oligodendrocytes. Physical deformation of axons can cause failure of ion channels, changing membrane permeability and producing a conduction block that rapidly reverses when decompressed. Ongoing spinal cord compression can also cause development of syringohydromyelia cranial to the compression site, potentially causing neuropathic pain in addition to further neurological deterioration.

Instability

Instability of the vertebral column can have devastating consequences for the patient. Sudden luxation of an unstable vertebral unit can cause spinal cord transection, contusion and compression (**302**). Sometimes, apparently stable fractures/luxations have just enough movement to cause repeated small spinal cord contusions, producing a deterioration in neurological status. Stability is produced by the interaction of the vertebrae with each other via intervertebral discs and synovial joints at the articular facets. The dorsal and ventral longitudinal ligaments, interarcuate ligaments and spinal musculature provide further support. While there are different methods of predicting instability, the most commonly used method divides the spine into three compartments (**303**). Compartment one contains the ventral three-quarters of the vertebral body and disc, and the ventral longitudinal ligament; the second compartment consists of the dorsal one-quarter of the vertebral body, the disc and the dorsal longitudinal ligament; and the third compartment includes the articular facets, lateral pedicles, dorsal laminae, interarcuate ligaments and dorsal spinous processes. Disruption of any two of the three



▲ 302 Lateral radiograph and sagittal T2-weighted MR image (inset) of the thoracolumbar spinal column of a dog that was hit by a car. The fracture and displacement of the first lumbar vertebra have caused severe mechanical damage to the spinal cord.



▲ 303 Lateral radiograph of the lumbar spine showing the three compartments that are evaluated when determining stability of the spine.

compartments is suggestive of instability. Sometimes, muscle spasm or impaction of fracture fragments into each other renders a potentially unstable injury stable for practical purposes. It is also important to remember that disruption of the soft tissues of the intervertebral disc, the dorsal and ventral longitudinal ligaments and the synovium of the articular facets disrupts all the compartments and causes instability.

CLINICAL PRESENTATION

Animals with spinal trauma can present with a range of signs depending on the location and severity of the injury. Mild injuries may just cause spinal pain, but more severe injuries cause neurological deficits related to the location (see Chapter 1). The aneurological examination aims to localize the neurological injury and to grade its severity. Special attention should be paid to determining the presence of voluntary motor function and nociception in each limb. In cases of suspected sacrocaudal fracture or luxation, nociception in the tail base and perineal region should be assessed. It is not unusual for there to be more than one site of injury and so neurological signs can be multifocal, and peripheral nerve injury, such as brachial plexus avulsion, can complicate the clinical assessment. A full neurological assessment should be performed cautiously, as clinical deterioration is possible due to vertebral instability. Such a deterioration can be catastrophic, particularly in patients that have suffered an atlantoaxial injury. It should be remembered that toy breeds can develop atlantoaxial instability secondary to minor trauma due to congenital malformations of the dens and associated ligaments.

Patients who have suffered trauma can have other soft tissue injuries. It is not uncommon for spinal trauma victims to have significant thoracic trauma causing pneumothorax, pulmonary contusions and traumatic myocarditis with their attendant signs. In addition, cervical spinal cord injury may affect motor control of the intercostal and diaphragmatic muscles. The ability to ventilate should therefore be assessed carefully. Abdominal trauma can result in a ruptured bladder and splenic and hepatic injury. Finally, neurological signs can be masked by appendicular fractures and complicated by head injury.

DIFFERENTIAL DIAGNOSIS

In the absence of a history of trauma, the following differentials should be considered: acute intervertebral disc herniation; vascular disease of the spinal cord or affecting the blood supply of the limb (ischaemic neuromyopathy); pathological fracture associated with neoplasia, infection or metabolic disease.

DIAGNOSIS

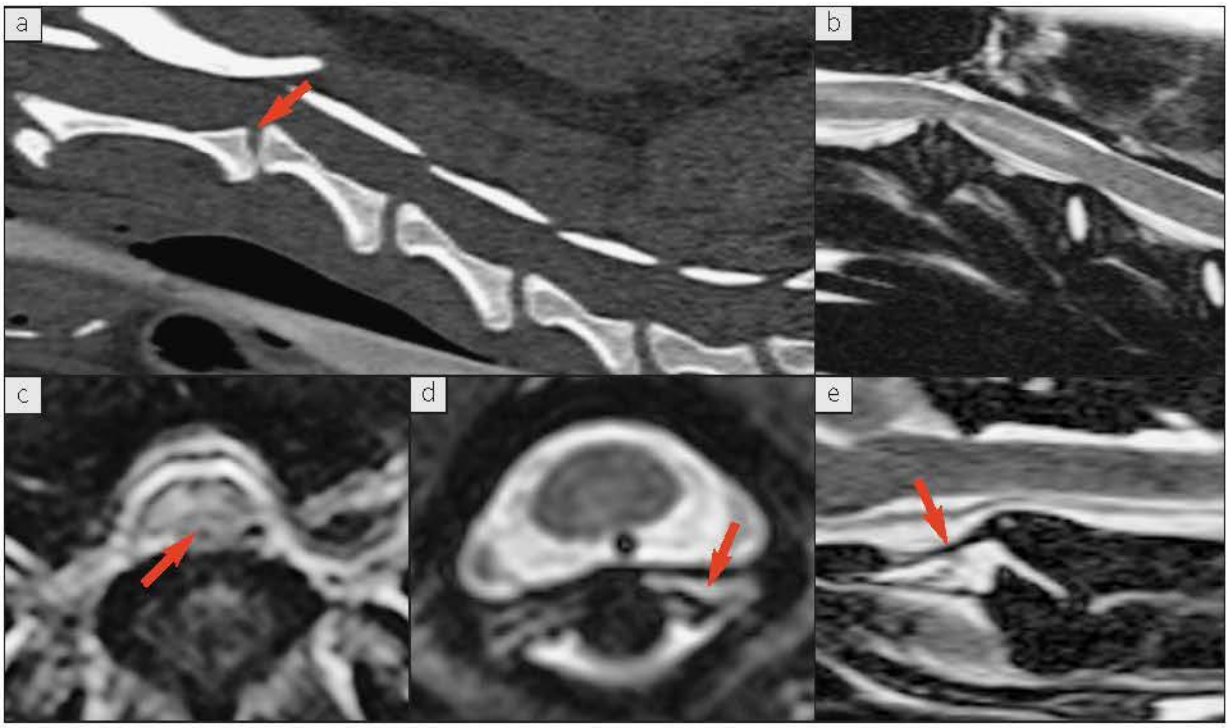
Diagnosis is confirmed by imaging of the spine. Imaging also provides information on the number and location of lesions and on the type of injuries that are present (compression, contusion, instability), thus allowing the clinician to make an appropriate treatment plan. Following systemic stabilization of the injured patient, the first diagnostic step is to obtain spinal radiographs. The entire spine should be radiographed, notwithstanding the presenting signs, because of the possibility of clinically silent lesions and an LMN-type lesion masking the effect of a UMN lesion. Thoracic and abdominal radiographs should also be obtained to identify additional soft tissue injuries.

Great care should be taken with moving and positioning the patient because of the possibility of instability. Two people should always be present so that the patient can be moved while providing adequate support to the spine. Sedation is needed to position adequately and for pain control (see Chapter 30 for further details), but should be administered cautiously as muscle relaxation increases the risk of further instability. Lateral views are taken first and evaluated for evidence of fractures or luxations. Orthogonal views should always be obtained. Ideally, a horizontal beam is used to obtain the ventrodorsal views. If this is not possible, the patient should be rolled onto its back very carefully with adequate support. The radiographs are evaluated for evidence of fractures, luxations, subluxations and collapsed disc spaces. The presence of displaced fracture fragments is important to note, as this indicates compression is likely. The radiographs should be evaluated for evidence of instability based on the three compartment model (see above). In the case of suspected AA instability, if a subluxation is not visible on lateral radiographs, the cervical spine can be flexed carefully while fluoroscoping the procedure to identify instability. Flexion of the neck without fluoroscopic monitoring is not appropriate, as it could result in catastrophic failure of the AA junction.

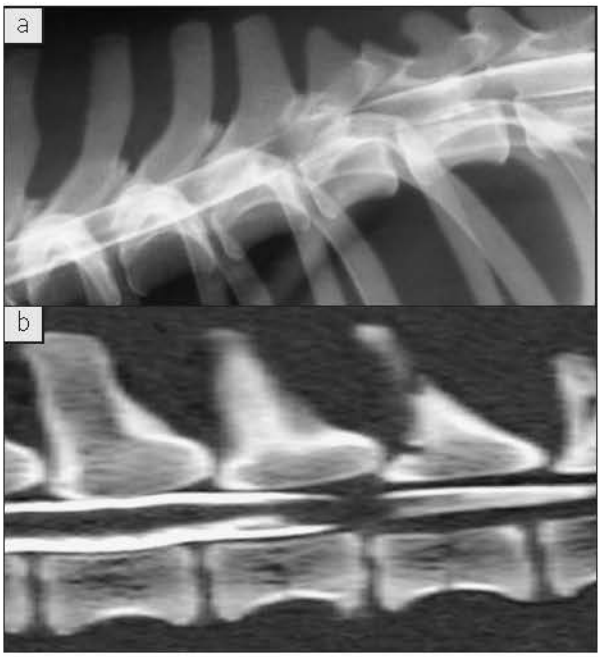
Further evaluation of the injured spinal cord following trauma requires advanced imaging. This is vital if surgery is planned, but not necessary in mildly affected animals that are going to be managed conservatively. Advanced imaging will require anaesthesia and this will require that the patient is stable with respect to its respiratory and cardiovascular systems. CT and MRI are the preferred modalities and both have advantages and disadvantages. CT provides excellent detail of fracture fragments and can identify fractures that are not visible on plain radiographs. Moreover, three-dimensional reconstruction of images is possible, greatly facilitating surgical planning (**304**). However, CT provides less information on the soft tissue components of the injury and might therefore miss compressive lesions due to haematomas or intervertebral disc material. MRI provides excellent soft tissue detail, identifying spinal cord contusions, disc herniations and epidural haemorrhage, but it can be more difficult to identify fracture lines in vertebrae, which is important information when planning 'corridors' for implant placement (**305**). Both CT and MRI are useful for measuring vertebral body size from the transverse views, essential when considering the maximum depth of surgical implants to be used.



▲ **304** **A three-dimensional reconstruction of a cervical column CT scan demonstrating a locked facet on the left side of the subluxated C5/C6 vertebrae (arrow). Such images are crucial for the correct surgical planning of many spinal fractures and luxations. (Photo courtesy Simon Platt)**



▲ 305 CT and MR images of a dog with a C2/C3 spinal luxation and traumatic disc herniation. The sagittal reconstruction of the CT image (a) shows a collapsed disc space at C2/C3 with mild dorsal displacement of the cranial end of the C3 vertebral body (arrow). The sagittal T2-weighted MR image (b) shows hyperintensity in the spinal cord parenchyma centered on C2/C3 and extending for the length of both vertebrae, indicative of a spinal cord contusion. The transverse T2-weighted image at the C2/C3 disc interspace (c) shows herniated disc material causing compression of the overlying spinal cord (arrow). The transverse and sagittal T2-weighted images at the level of C1/C2 (d, e) show that the transverse ligament of the dens is intact, although it contains a region of hyperintensity, perhaps indicative of a tear (arrow) (d) and that the apical ligament of the dens is also intact (arrow) (e).



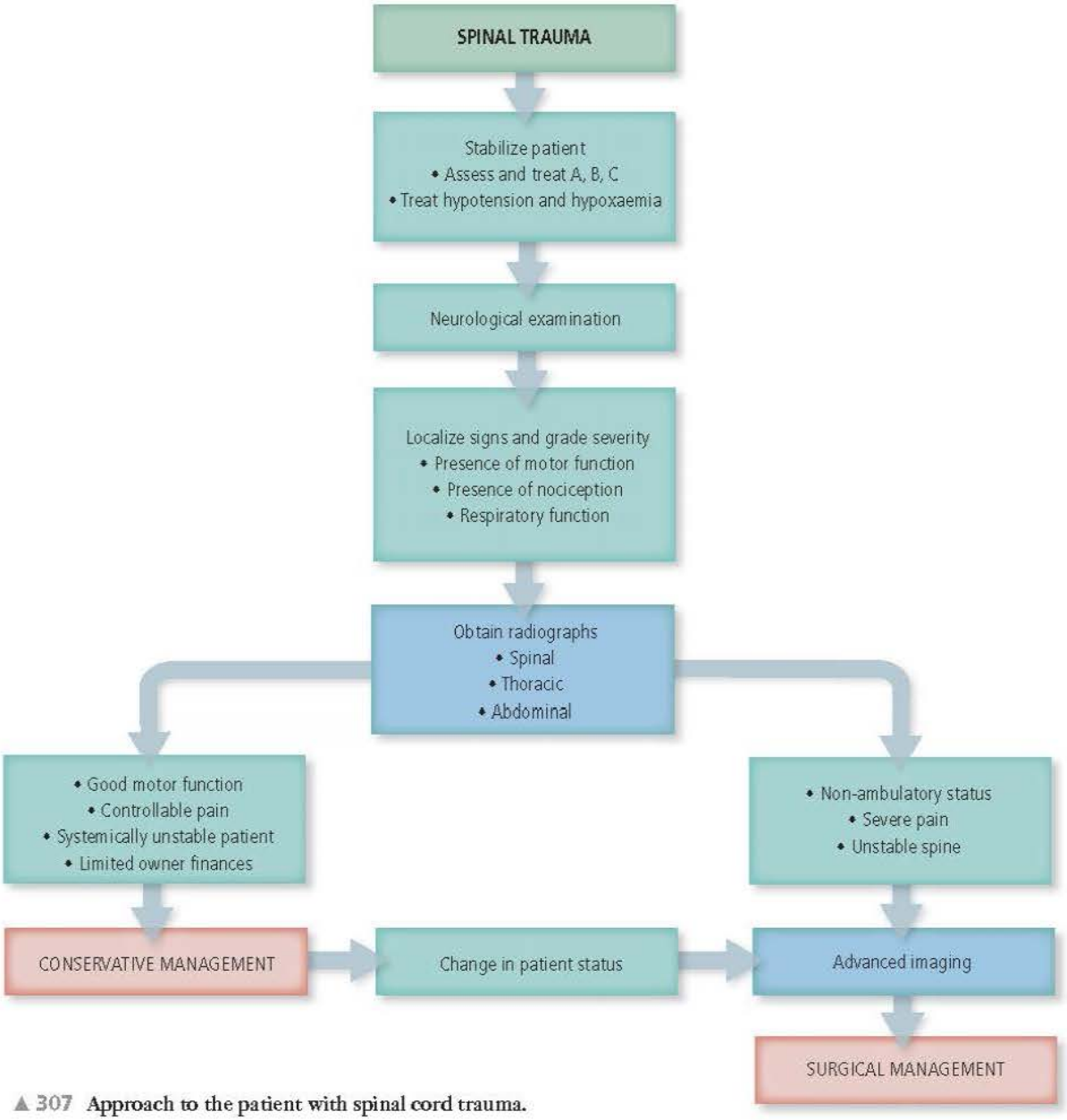
▲ 306 (a) Lateral myelogram of the thoracolumbar spine of a patient with a traumatic injury at T10/T11. Note the slight collapse of the disc space, with thinning of the contrast columns at T10/T11 and over the body of T11. (b) Lateral CT myelogram of the lumbar spine of a dog following a trauma that caused an L5/L6 subluxation. Dorsal and ventral attenuation of the subarachnoid contrast columns is notable at the site of the luxation, suggestive of a circumferential compressive lesion. (Photo courtesy Simon Platt)

Myelography as a diagnostic technique has largely fallen out of favour because of the potential to cause deterioration in neurological signs and potential side-effects such as seizures. Because patients with spinal fractures and luxations frequently have vertebral instability, the potential for causing additional injury during positioning to obtain orthogonal views in myelography is of real concern. However, historically, myelography has been used to identify spinal cord compression, and it can be used when CT and MRI are not available. Myelography can also be combined with CT to enhance the ability to identify soft tissue compression of the spinal cord (**306**).

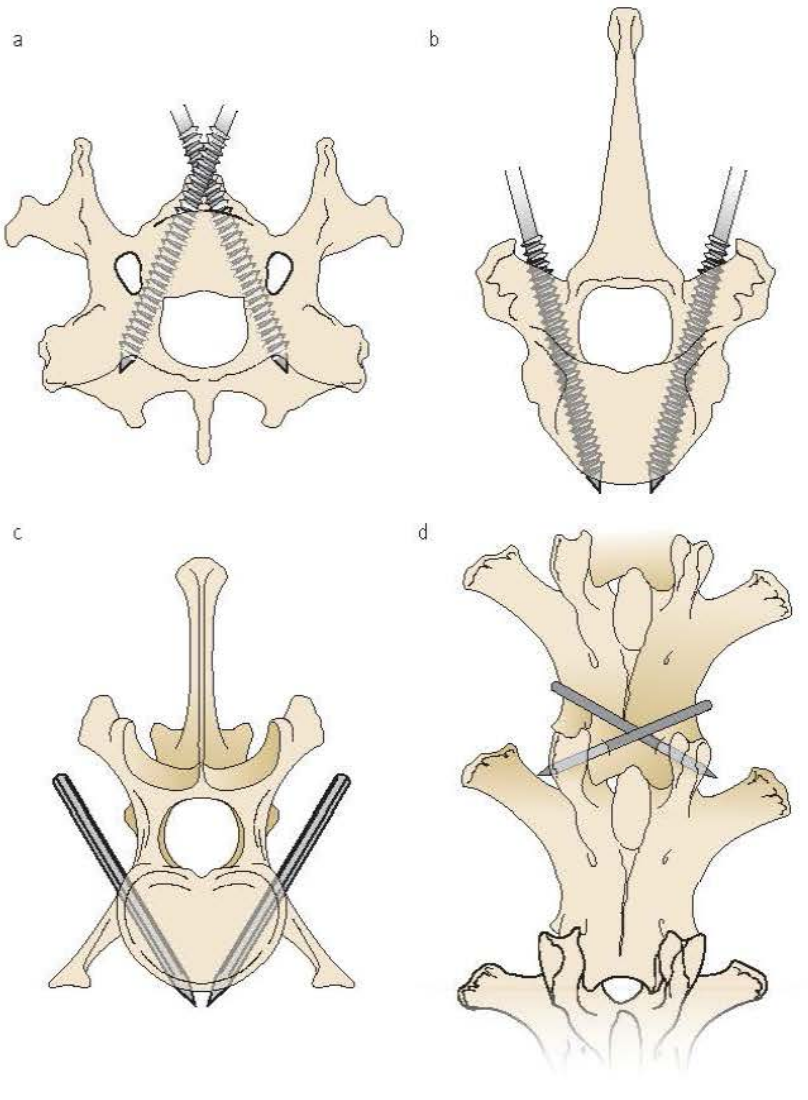
MANAGEMENT

Treatment of spinal trauma is focused on contusion, compression and instability. The decision to manage spinal trauma medically or surgically for these issues depends on the systemic and neurological examinations, as well as the findings of imaging investigations (**307**).

- **Contusion.** As with any trauma patient, the first step is to check airway patency, breathing and circulation. Hypotension and hypoxaemia will worsen the outcome of spinal cord injury and should be corrected if present. Further medical management is contentious. Corticosteroids may be indicated for shock, but are not indicated to treat spinal cord injury. Methylprednisolone sodium succinate (MPSS) has been advocated as a free radical scavenger. Prospective placebo-controlled trials in humans with spinal cord injury (the National Acute Spinal Cord Injury Study [NASCIS] trials) suggested that high doses of MPSS (30 mg/kg IV followed by a CRI of 5.4 mg/kg/hour for 24–48 hours) improved outcome slightly if treatment was initiated within 8 hours of injury. Since the publication of the NASCIS trials, the validity of the statistical analysis and conclusions of the study have been questioned and the results remain contentious. MPSS did not improve outcome in dogs with an experimentally induced spinal cord injury, and there are no controlled data on its effect in a clinical setting. There is currently no clear evidence that MPSS will improve outcome of spinal cord injury in dogs. Polyethylene glycol (PEG) has also been advocated as a therapy for acute spinal cord injury. This hydrophilic polymer is a surfactant that can seal defects in cell membranes. Following injury, membrane damage causes an increase in permeability that plays a large role in secondary injury. It is proposed that administration of PEG can reverse this change, thus improving outcome. A study in dogs with disc herniations showed that it is a safe drug and may improve outcome, but the outcomes reported in this study were similar to those in other published case series in which PEG was not administered. The drug is not commercially available in a medical grade at the time of writing, therefore it requires specialized pharmacy



▲ 307 **Approach to the patient with spinal cord trauma.**



◀ 308 Schematic representations of approximate pin or screw placement angles in (a) the body of the cervical vertebrae, (b) the body of the thoracic vertebrae, (c) the body of the lumbar vertebrae and (d) in the joint processes. The last represents a temporary fixation technique securing vertebral alignment prior to more appropriate implant use in the bodies of the vertebrae.

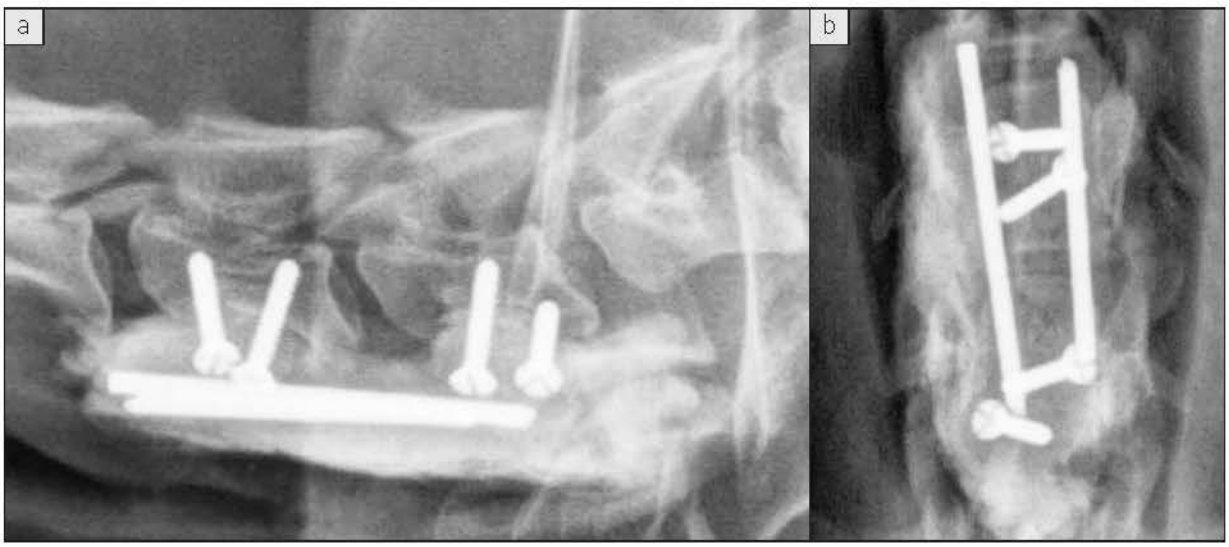
preparation and administration through a filter. The recommended dose is 2 ml/kg of PEG (3 500 Dalton, 30% w/w in saline) given intravenously over 15 minutes and then repeated 4 hours later. New adjunctive medical therapies are constantly being tested: minocycline and erythropoietin show promise, but they have yet to be evaluated clinically.

- **Compression.** Compression of the spinal cord can be addressed surgically. Compression can be due to displaced vertebral fragments, a herniated intervertebral disc or haematomas. Decompression may be achieved by realignment of vertebrae alone; a laminectomy or hemilaminectomy may be necessary to remove material from the vertebral canal. Decompressive procedures could produce or exacerbate instability in the injured spine, thus requiring surgical stabilization.
- **Instability.** Instability can be addressed surgically, by placement of an external splint or simply by cage rest (*Table 85*). Surgical stabilization is the most effective method of stabilizing an unstable spine, but it is associated with significant surgical risks. A variety of different techniques are used. In one of the most easily adaptable techniques, screws or pins are placed in the vertebral bodies adjacent to the injury and cement is applied to hold the structure in alignment (**308, 309**). Another popular technique, sometimes known as 'spinal stapling' or 'segmental

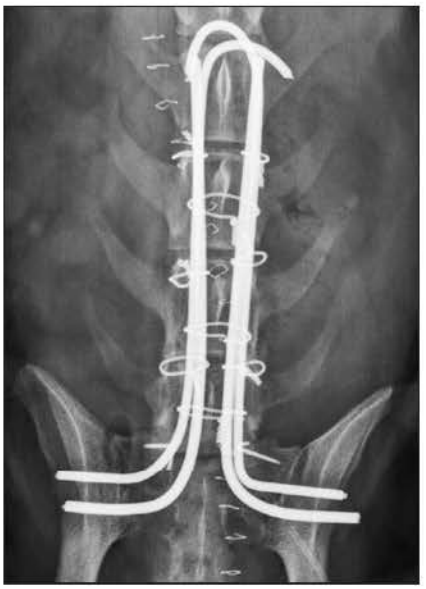
Table 85 **Advantages and disadvantages of different stabilization techniques**

TECHNIQUE	ADVANTAGES	DISADVANTAGES	INDICATIONS
Cage rest	Inexpensive No anaesthetic or surgical risk	No stability provided No decompression	Stable fracture (articular facet, dorsal spinous and transverse processes) No spinal cord compression Mild neurological deficits
External splint	Inexpensive No anaesthetic or surgical risk	Splint complications Limited protection against axial or rotational forces No decompression	Unstable fracture Limited spinal cord compression Mild neurological deficits
Screws/pins and PMMA; plates	Excellent stabilization Can combine with decompression	Cost Risk of iatrogenic injury during implant placement Infection Implant failure	Unstable fractures
Segmental stabilization	Good stabilization against flexion and extension Reduced risk of iatrogenic injury Readily applied in the lumbosacral region	Suboptimal protection against rotational and axial forces Implant failure/migration Infection	Unstable lumbosacral/caudal lumbar fractures

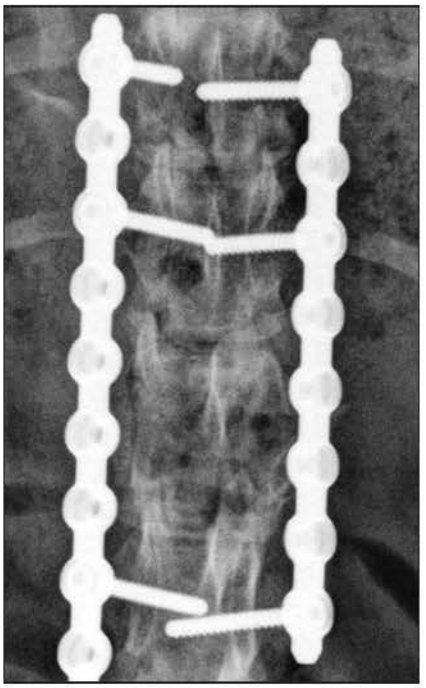
PMMA = polymethyl methacrylate cement



▲ 309 **Lateral (a) and ventrodorsal (b) radiographs of the cervical spine following surgical stabilization. The cervical luxation has been stabilized using screws and polymethyl methacrylate cement. K wires have been placed in the cement as rebars to strengthen the cement.**



▲ 310 Ventrodorsal radiograph demonstrating segmental stabilization of an L7 fracture. (Photo courtesy Karen Muñana)



▲ 311 Ventrodorsal radiograph of the thoracolumbar spine showing use of String of Pearls plates to repair an L1 fracture. (Photo courtesy Peter Early)

stabilization', uses pins wired to articular facets and dorsal spinous processes to stabilize dorsally (**310**). Different plates can be used. Difficulty contouring plates to the vertebral bodies limits options, but more recently, locking plates, such as the String of Pearls plate, have been described that can offer more flexibility (**311**).

Sacrocaudal luxations in cats are typically addressed by amputation of the tail if it is paralysed and has no nociception. Prompt removal of the tail may limit any ongoing damage to the sacral nerve roots that could result from inadvertent movement of the tail.

Surgical complications from any spinal stabilization procedure can be serious and include iatrogenic injury to the spinal cord, damage to the vasculature immediately ventral to the vertebral column and infection. The timing of surgery is often dictated by the severity of other systemic injuries (e.g. lung contusions, traumatic myocarditis), which might affect the ability to perform general anaesthesia. Typically, spinal stabilization is performed as soon as it is safe for the patient. However, animals with cervical injuries that are hypoventilating need surgery as soon as possible to avoid the use of, or reduce the amount of time spent on, a ventilator.

If surgery is not an option, patients can still make a successful recovery with conservative management. This involves strict confinement to a cage for 4–6 weeks combined with controlled rehabilitation exercises. If there is an unstable fracture or luxation, an external splint can be placed. The fore- and hindlimbs need to be included in the splint in order to immobilize the thoracolumbar junction, and the head and forelimbs must be included to immobilize the cranial cervical spine (**312**). Placement of the splint is achieved by wrapping the appropriate part of the body in cast padding. A splint is then formed (e.g. from Vetcast [3M]) to cover the dorsal aspect of the thoracolumbar spine or the ventral aspect of the neck (from below the chin to the sternum). Following padding of the splint to ensure that there are no sharp edges, it is incorporated into the bandage with a cover of bandaging material such as Vetwrap. Pressure points, particularly between the fore- and hindlimbs, should be checked and padded carefully. The patient should always be hospitalized overnight after the first placement of a splint to ensure that it is tolerated and to allow adjustment for any initial



▲ 312 Application of an external splint for a caudal lumbar fracture luxation. (Photo courtesy Simon Platt)



▲ 313 A partial thickness decubital ulcer present over the ischiatic protuberance (arrow) in a dog that had been recumbent for 2 weeks.

splint movement. Splints should be checked daily by the owner for development of decubital ulcers. They should be checked and potentially changed by the veterinarian after the first 3–5 days, then on a weekly basis for 6 weeks. Splints do not protect from compressive loading of the spine and offer poor protection against rotatory forces. In addition, it is not possible to stabilize the lumbosacral spine with an external splint. Splints are inappropriate if there are open wounds affecting areas that would be incorporated into the bandage.

Aftercare of all patients is similar whether managed surgically or conservatively. Pain relief should be provided. An appropriate regimen includes:

- An NSAID such as carprofen (contraindicated if large doses of corticosteroid have been administered).
- An opioid (e.g. intravenous hydromorphone in the first 24–48 hours, then oral tramadol or transdermal fentanyl).
- A drug active against neuropathic pain (e.g. gabapentin).

Animals should be confined to a small, well-padded cage so that they cannot fall. They should be taken out 3–4 times a day to urinate (or have their bladder manually expressed) and defecate and for limited controlled and supported exercise. Massage and PROM exercises should be performed on affected limbs to maintain the integrity of joints and muscles. Ideally, patients are managed initially at a rehabilitation centre or a rehabilitation plan is developed for the owner to perform at home. If the patient is unable to urinate, the owner must be able to express or catheterize their pet 3 times a day. The addition of phenoxybenzamine (0.25–0.5 mg/kg PO q8–12h) or prazosin (dog: 1 mg if less than 15 kg body weight or 2 mg if over 15 kg PO q8–12h; cat: 0.25–0.5 mg PO q12–24h) and diazepam (0.5 mg/kg PO 20 minutes prior to expression) may help to reduce urethral sphincter tone and facilitate expression. Since marked hypotension can result from prazosin, patients should be monitored for lethargy, collapse, pallor, syncope or seizures. The skin should be kept clean and dry and checked regularly for development of urine scald or decubital ulcers over pressure points (**313**). Patients should be rechecked by the veterinarian at least once a week if a splint has been applied; they are expected to make a steady recovery. Any deterioration in neurological status should be investigated using spinal radiography and, potentially, advanced imaging if deterioration continues. At 6 weeks, the splint can be removed and the owner instructed to gradually increase the amount of controlled exercise that the patient performs over the next 3 months. Vigorous exercise that involves jumping and twisting should be avoided permanently, especially in the case of luxations, which will only demonstrate fibrous union rather than osseous union.

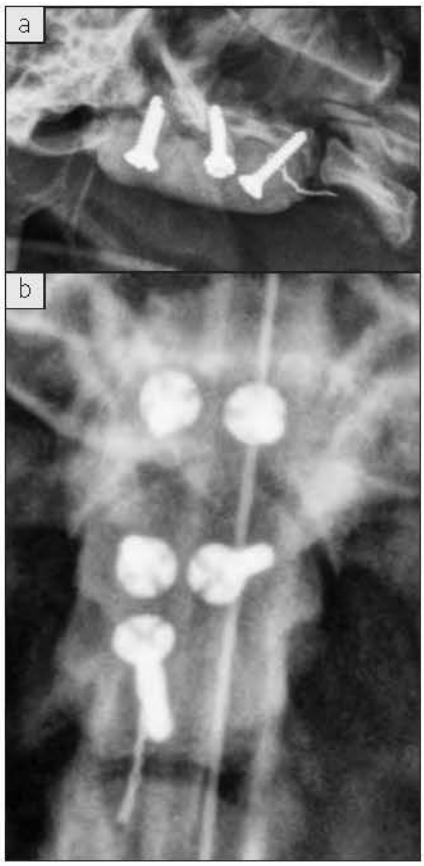


▲ **314** Lateral (a) and ventrodorsal (b) radiographs of surgical correction of an atlantoaxial instability using two screws placed transarticularly between C1 and C2. The cartilage between C1 and C2 was removed and an autologous cancellous bone graft placed to produce bony fusion. A splint was placed for 6 weeks postoperatively.

Management of atlantoaxial subluxation

AA subluxations pose a particular set of therapeutic problems that include extremely small and soft bones due to breed and age, high risk of mortality associated with the consequences of a C1/C2 spinal cord injury and a difficult surgical approach. Cases can be managed surgically or conservatively, but in general, surgery is recommended for any patient with a severe luxation (and therefore instability) and neurological deficits. A variety of different surgical techniques have been advocated. A ventral approach is used most commonly nowadays, although great care should be taken of the soft tissue structures (the larynx, pharynx, oesophagus and thyroid glands) retracted to give access to the ventral aspect of the cervical spine. Screws or threaded pins can be placed transarticularly between C1 and C2 (**314**), although it can be difficult to achieve the necessary angle and bone failure may also occur in young toy breeds. An alternative is to place screws vertically in the body of C1 and C2 and encase them in polymethyl methacrylate cement (**315**). Using the latter approach, placement of the screws still requires careful consideration of the implant corridors, but it is more straightforward than placing transarticular screws. The disadvantage is that the cement lying ventral to C1/C2 can cause compression of the underlying pharynx and airways, resulting in swallowing difficulties. The immediate postoperative period carries a high risk of respiratory failure and cases should recover in an intensive care unit in which they can be monitored closely and placed on a ventilator if needed. The prognosis for recovery following surgery is affected by the severity and duration of signs at presentation and the age of the dog. It is also important to note that surgical experience and skill can critically affect the outcome, and this surgical procedure should not be attempted without appropriate training.

Conservative therapy of AA subluxation is indicated in dogs that are extremely young, in order to postpone surgery until a time when their skeleton is more mature, in dogs with a fracture and mild signs (pain, paresis only), and in cases where the owner is reluctant for surgery to be performed. An external splint is placed that extends from in front of the ears to include the forelimbs. The neck is placed slightly in extension. The splint in kept in place for 6–12 weeks. An animal with a fracture can develop a bony union within 6 weeks and may have the splint removed at that time if radiographs show fusion. Animals with congenital instability may not be able to stabilize their AA junction permanently with conservative therapy. It is hoped that scar tissue will form between the dorsal aspect of C1 and C2 (the dorsal AA ligament) and potentially around the dens while in the splint. However, although most dogs will improve while the splint is in place, this fibrous repair will always be prone to further damage and a relapse in signs is possible.



▲ 315 Lateral (a) and ventrodorsal (b) radiographs of surgical correction of an atlantoaxial instability using two screws placed in the ventrum of C1, two screws in the cranial body of C2 and one screw placed in the caudal body of C2. The caudal screw was placed to aid in the reduction of the subluxation. A wire was placed around the screw and retracted caudally to hold the vertebrae in alignment while the polymethyl methacrylate cement was placed and hardened around the screw heads. As in 314, the cartilage between C1 and C2 was removed and a bone graft was placed to produce bony fusion. There is no need for a postoperative splint using this technique.

PROGNOSIS

The prognosis associated with spinal cord injury is influenced by the severity of the spinal cord injury and the presence of injuries to other organs (e.g. lungs, heart, bladder). The form of treatment (surgical versus conservative) does not appear to influence outcome, although in published case series the more severely affected patients tend to be treated surgically, and so a true comparison is difficult. Prognostic indicators based on the neurological examination are somewhat different for different regions of the spine:

- Thoracolumbar injuries carry a guarded to grave prognosis for recovery of hindlimb function and faecal and urinary continence if the animal is paraplegic with loss of nociception to its hindlimbs. If nociception is still present, these animals do have a good chance of recovery.
- Cervical injuries are associated with a guarded to grave prognosis if the animal is tetraplegic and unable to ventilate adequately. If treated surgically, the risk of perioperative death can be as high as 36% in cervical injuries. Note that it is extremely unusual to see tetraplegic animals that lack nociception, because cervical spinal cord transection usually causes death by respiratory failure and bradyarrhythmias. Delaying referral, diagnosis and treatment does worsen the prognosis. Less severe injuries carry a much better prognosis, with the majority of cases making a recovery if managed appropriately.
- The prognosis for recovery of faecal and urinary continence in lumbosacral and sacrocaudal fractures is approximately 50% if there is absent anal tone and no nociception in the perineal region or the tail at the time of presentation. A recent study suggests that positive tail base sensation is useful for identifying cases that will definitely recover within 30 days of the injury, but it is not very useful for identfying cases that will recover despite not having tail base sensation. Because the cauda equina is largely composed of peripheral nerves, displacement of fracture fragments is less likely to cause complete transection, but severe pain due to nerve root entrapment is common and can be a reason for euthanasia.

ACUTE DISC DISEASE

Joan Coates

INTRODUCTION

Degenerative disc disease represents clinical signs related to degenerative changes in the intervertebral disc. Fibroid degeneration of the disc is a normal age-related change associated with progressive decrease in proteoglycans and glycosaminoglycans. These degenerative changes are accelerated in the chondrodystrophic breeds.

Intervertebral disc disease (IVDD) is often divided into two distinct categories, referred to as Hansen type I and Hansen type II:

- Hansen type I IVDD results in herniation of the nucleus pulposus through the annulus fibrosus and extrusion into the vertebral canal, and is usually associated with chondroid metaplasia.
- Hansen type II IVDD results in annular protrusion caused by shifting of central nuclear material and is associated more with fibroid degeneration.

Acute IVDD is characterized by rapid extrusion of nucleus pulposus into the vertebral canal causing spinal cord compression and extradural haemorrhage. As such, acute disc disease is usually synonymous with type I IVDD, but it can occur either without preceding disc degeneration (traumatic non-compressive nucleus pulposus extrusion) or following type II IVDD. This type of clinical presentation is caused by a combination of primary and secondary spinal cord injury. The spinal cord is the 'innocent bystander' and neurological dysfunction is a secondary consequence of disc herniation.

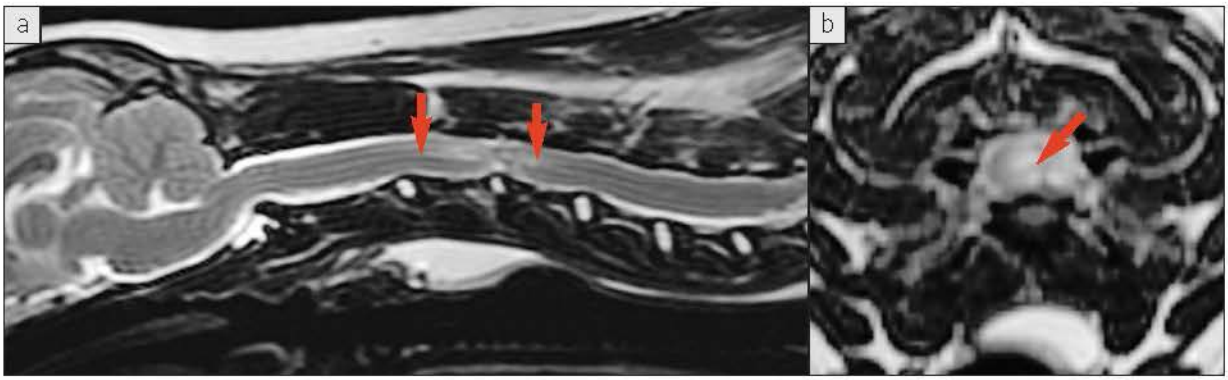
The cervical and thoracolumbar spinal cord are commonly affected by acute-onset Hansen type I IVDD. The presence of nociception in the limbs is a positive indicator for recovery from acute IVDD.

AETIOLOGY AND PATHOPHYSIOLOGY

The intervertebral disc permits stable motion of the spine while supporting and distributing loads under movement. The annulus fibrosus is a multilaminated ligament that encompasses the periphery of the disc and attaches to the hyaline cartilage of the vertebral end plates. Its outer collagen lamellae blend with the ventral and dorsal longitudinal ligaments, while the inner lamellae blend with the nucleus pulposus. The nucleus pulposus, an embryologic remnant of the notochord, is the central portion of the disc and is highly hydrated.

The major molecular components of the discs are collagenous and non-collagenous proteins, proteoglycan aggregates and glycoproteins. Glycosaminoglycans (GAGs) are proteoglycans composed of repeating units of hexosamines: chondroitin sulphate (CS), dermatan sulphate, keratan sulphate (KS) and hyaluronic acid. One of the functions of GAGs is to imbibe water. Concentrations of these GAGs are highest in the nucleus pulposus. Age-related or pathological change is associated with a progressive decrease in GAG content coinciding with a decrease in water and proteoglycans within the nucleus and annulus. The proportion of non-collagenous proteins also increases with age: the structure of the aggrecan changes, the core protein and GAG chains shorten and there is an increase in the ratio of KS to CS. CS synthesis differs from KS synthesis in the requirement of oxygen during the constituent sugar formation. Thus, the increased KS:CS ratio is a consequence of the change from an aerobic to an anaerobic environment.

These degenerative changes occur earlier in chondrodystrophic breeds. The intervertebral discs of these dogs undergo chondroid metamorphosis as early as 2 months after birth. Chondrification involves a decrease in GAGs and an increase in collagen. Studies on structural composition of the nucleus pulposus and the transitional zone suggest a genetic predisposition for IVDD.



▲ **316** **T2-weighted MR mid-sagittal (a) and transverse (b) images of a cervical spine from a Pomeranian with acute-onset tetraparesis from a suspected acute non-compressive nucleus pulposus extrusion. An area of intraparenchymal hyperintensity (arrows) suggestive of oedema or ischaemia extends from C3 to C4. There is dorsal displacement of the nucleus pulposus within the interspace and minimal spinal cord compression.**

Hansen first classified IVDD as type I and type II. Hansen type I IVDD is herniation of the nucleus pulposus through the annular fibres and extrusion of nuclear material into the vertebral canal. The extrusion causes dorsal, dorsolateral or circumferential compression of the spinal cord. Acute disc extrusion is characterized by extradural haemorrhage and soft disc material. Hansen type II IVDD is characterized by annular protrusion caused by shifting of central nuclear material and is commonly associated with fibroid disc degeneration associated with age-related changes in the disc constituents. Acute-onset disc disease is less common with Hansen type II IVDD. A third type of IVDD has been described as acute non-compressive nucleus pulposus extrusion (ANNPE). Other terms include high-velocity–low-volume disc extrusion, intervertebral disc 'explosion' and traumatic disc extrusion. However, the term ANNPE describes the main features of the disease and helps differentiate it from the more common type of disc extrusion that occurs following intervertebral disc degeneration (Hansen type I IVDD) and that typically results in spinal cord contusion and compression (**316**).

Extrusion of the nucleus or protrusion of the annulus causes primary spinal cord injury and associated neurological signs by concussion, compression, laceration and ischaemic events. Spinal cord damage is usually most severe at the site of intervertebral disc protrusion or extrusion. Pathological changes are characterized as compressive myelopathy and myelomalacia with demyelination of the ventral, lateral and dorsal funiculi. Wallerian degeneration occurs in the spinal cord segments above and below the lesion in the ascending and descending pathways, respectively. An inflammatory reaction subsequently develops as a result of the neurodegenerative and injury processes.

Acute and severe disc extrusions cause pannecrosis of the grey and white matter. Sequential haemorrhage, oedema and neuronal necrosis depend on severity and type of injury. Acute spinal cord injury initiates a cascade of vascular, ionic and biochemical events, associated with ischaemia, that contributes to secondary spinal cord injury and irreversible neuronal damage. Myelopathic changes initially involve the grey matter, with centrifugal spread to the white matter.

The most severely affected dogs (paralysis with absent nociception) develop ascending and descending haemorrhagic myelomalacia, which is an auto-destructive myelopathy. This type of myelomalacia is suspected to be an end-stage result of ischaemic and circulatory processes. Its pathogenesis is unknown, but it is thought to reflect extensive compromise of the intramedullary vasculature with haemorrhagic or non-haemorrhagic infarction. Haemorrhage is often present in the extradural and subarachnoid spaces and spinal cord parenchyma. Myelomalacia extends from the site of impact to ascend or descend the spinal cord. Associated neurological signs include analgesia, areflexia, ascending cutaneous trunci reflex loss and respiratory dysfunction.

The incidence rate of focal and ascending/descending haemorrhagic myelomalacia has been reported to be as high as 10% in dogs with acute thoracolumbar IVDD and loss of nociception. Myelomalacia is also not an uncommon scenario with traumatic non-compressive disc extrusions where the extruded nucleus spreads along the epidural space for a distance and may completely surround or penetrate the dura mater. The prognosis for ascending and descending haemorrhagic myelomalacia is generally poor; however, there have been reports of improvement in neurological function in cases of focal malacia.

Hoerlein determined that IVDD accounted for 2.02% of all diseases diagnosed in dogs. Thoracolumbar IVDD accounts for approximately 80–85% of all disc lesions, with the highest incidence being at the thoracolumbar junction (T12/T13 to L1/L2) in chondrodystrophic dogs. The Dachshund has the highest frequency followed in succession by the Pekingese, Welsh Corgi, Beagle, Lhasa Apso and Miniature Poodle. Large non-chondrodystrophic breeds of dog (e.g. Doberman Pinscher, German Shepherd Dog, Dalmatian and Labrador Retriever) are also affected with Hansen type I IVDD. The most common site in large breed dogs is the disc interspace between L1 and L2. The age at onset for clinical signs of thoracolumbar IVDD peaks at 4–6 years of age in chondrodystrophic breeds and at 6–8 years in non-chondrodystrophic breeds. Cervical IVDD accounts for approximately 15–20% of all intervertebral disc extrusions. The most common sites for Hansen type I IVDD in the cervical spine are C2/C3 and C3/C4 in small breed dogs and C6/C7 in larger breed dogs.

CLINICAL PRESENTATION

Neurological signs seen in dogs with IVDD may be peracute (<1 hour), acute (<24 hours) or subacute (>24 hours). Hansen type I IVDD is the most common cause for the peracute and acute clinical presentations of IVDD. Clinical signs of intervertebral disc extrusion are variable and determined by the rapidity and severity of spinal cord injury and neuroanatomical localization. The presence or absence of nociception determines the prognosis.

Cervical intervertebral disc disease

Cervical spinal pain is the most common clinical sign of acute-onset cervical IVDD. Low head and neck carriage, neck guarding, stilted gait, radicular pain and spasms of the cervical spinal muscles are common clinical manifestations of cervical spinal pain. Due to the greater ratio of the vertebral canal diameter to spinal cord diameter in the cervical spine, Hansen type I cervical disc disease commonly presents with pain only even if a large amount of nucleus is extruded. Pressure from disc material on the nerve root can cause nerve root ischaemia and severe pain. Pain is often intermittent and manifests as forelimb lameness (root signature or radicular pain). Radicular pain also can be elicited by manipulation of the affected limb. Gait evaluation is assessed as normal, GP ataxia (more severe in the hindlimbs) and hemi- or tetraparesis/plegia. Neurological dysfunction can be asymmetric based on lateralization of the extruded disc. In general, forelimb spinal reflexes are normal to hyperreflexic with a C1–C5 spinal cord lesion and normal to hyporeflexic with a C6–T2 lesion. However, spinal reflex evaluations may not be reliable for neuroanatomical localization within the cervical spinal cord region following acute disc disease. A decreased withdrawal reflex does not always indicate a lesion from C6–T2 and it can also occur with lesions at the C1–C5 spinal cord level. Non-ambulatory tetraplegia is an infrequent clinical manifestation of cervical IVDD. A study of 32 dogs summarized that fewer than one-third of dogs that are non-ambulatory secondary to cervical disc herniation experience complete loss of voluntary motor function; sensory deficits are encountered even less frequently. Horner's syndrome can be a clinical manifestation caused by disruption of the tectotegmental spinal tract with severe cervical spinal cord injury. Loss of nociception is rare in dogs with acute cervical IVDD, but is associated with severe spinal cord damage, myelomalacia, cardiac arrhythmia and respiratory dysfunction.

Thoracolumbar intervertebral disc disease

Clinical signs of thoracolumbar IVDD vary from spinal hyperaesthesia only to paraplegia with or without nociception. Dogs with back pain only are reluctant to walk and may show kyphosis. Dogs with back pain alone or minimal neurological deficits can have imaging evidence of substantial spinal cord compression. Lateralization of the extruded disc and spinal cord compression will often

cause asymmetry of neurological deficits. Neuroanatomical localization of thoracolumbar spinal lesions is determined by normal to hyperreflexic (T3–L3) or hyporeflexic (L4–S3) spinal reflexes and by site of paraspinal hyperaesthesia. Dogs presented with peracute or acute thoracolumbar disc extrusions often manifest initial clinical signs of 'spinal shock' and/or Schiff–Sherrington postures. Spinal shock is usually manifested as flaccidity distal to the lesion. Likewise, the spinal reflexes are depressed to absent and the bladder may be flaccid, with urine retention and sphincter hypotonia. The cause of spinal shock is unclear. A transient decrease in limb tone may be due to loss of descending supraspinal input on the alpha-motor neurons and interneurons, along with an increase in segmental inhibition. Spinal shock is important to recognize in order to prevent erroneous lesion localization. These transient phenomena indicate acute and severe spinal cord injury, but do not determine the prognosis.

A classification scheme adapted from Griffiths describing hyperaesthesia, sensory and motor dysfunction and loss of micturition has been used as a functional grading system to provide treatment guidelines for thoracolumbar IVDD:

0 = Normal.
1 = Paraspinal hyperaesthesia only.
2 = General proprioceptive ataxia and/or ambulatory paraparesis.
3 = Non-ambulatory paraparesis.
4 = Paraplegia (intact nociception).
5 = Paraplegia with loss of nociception.

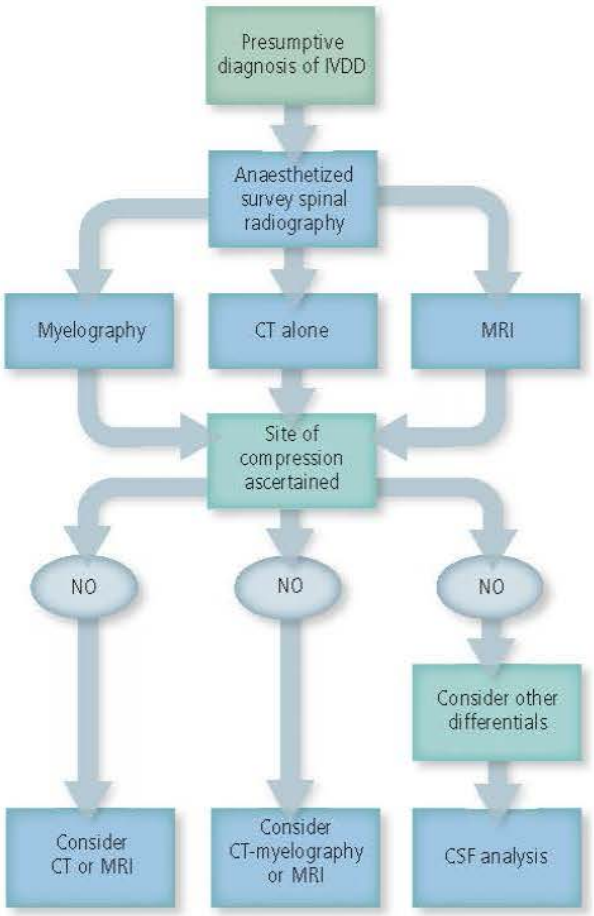
Complete loss of nociception is the most important prognostic indicator for acute spinal cord injury. Nociception by definition is perception of a noxious stimulus. Classically, a 'superficial' pain response is elicited on pinching a skin fold and a 'deep' pain response is elicited on use of a noxious stimulus, most commonly a bone of a digit. Distinguishing between superficial and deep 'pain' perception may not be reliable because of individual animal differences in perception of a 'painful' stimulus. Moreover, differences between these two nociceptive pathways are poorly defined.

Ascending and descending haemorrhagic myelomalacia should be suspected in dogs with thoracolumbar IVDD that have an ascending loss of the cutaneous trunci reflex. Other neurological signs of myelomalacia include loss of nociception caudal to the lesion, ascending and descending flaccidity and areflexia, tetraplegia, hyperthermia and respiratory distress. Death results from asphyxia associated with intercostal and diaphragmatic muscle paralysis. Clinical signs of ascending and descending myelomalacia may manifest in hours to several days from the onset of paraplegia.

DIFFERENTIAL DIAGNOSIS

A differential diagnosis for acute disc disease is based on speed of onset, lesion symmetry and presence of paraspinal hyperaesthesia. Paraspinal hyperaesthesia usually indicates a compression and/or inflammation to pain-sensitive structures, which include the periosteum of the vertebrae, meninges, nerve roots and superficial layers of the annulus fibrosus. Disorders that typically do not manifest paraspinal pain include intramedullary neoplasia and fibrocartilaginous embolic myelopathy (FCEM).

- **Vascular.** FCEM thrombosis, infarction.
- **Inflammatory.** Infectious: meningitis/myelitis (viral, fungal, bacterial, rickettsial, protozoal, algal), spinal epidural empyema, discospondylitis (bacterial, fungal), vertebral physitis. Noninfectious: MEM of unknown aetiology (granulomatous MEM, necrotizing encephalomyelitis), steroid-responsive meningitis, vasculitis.
- **Trauma.** Vertebral fractures/luxations, AA subluxation.
- **Neoplasia.** Primary: extradural (vertebral, lymphoreticular), intradural extramedullary (lymphoreticular, meningioma, nerve sheath tumour), intramedullary (oligodendroglioma, astrocytoma, ependymoma). Secondary: metastatic (lymphoreticular, haemangiosarcoma, meningeal carcinomatosis, undifferentiated sarcomas).
- **Degenerative.** Degenerative lumbosacral stenosis.



▲ 317 Neurodiagnostic technique decision-making scheme for diagnosis of acute intervertebral disc disease.

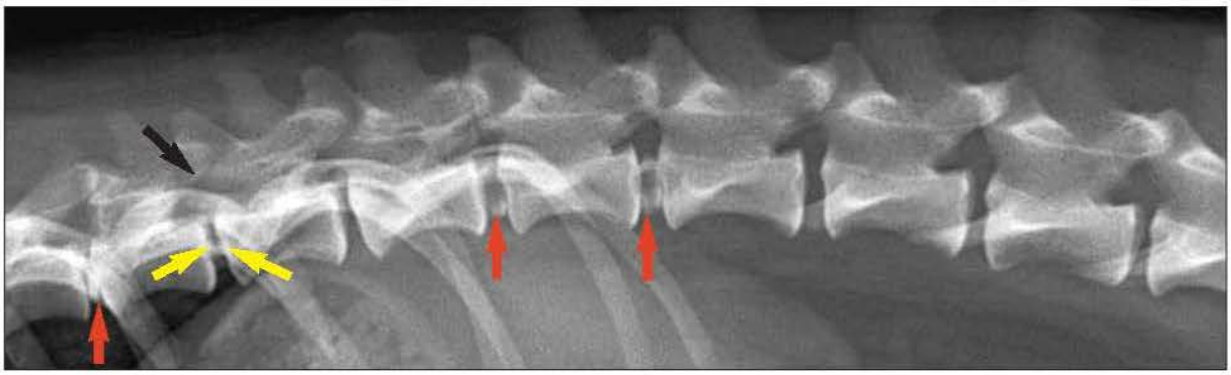
DIAGNOSIS

Imaging studies of the spinal cord (myelography and/or CT and MRI) are necessary to confirm the presence and extent of the lesion (**317**).

Survey radiography

Survey radiography identifies in-situ intervertebral disc mineralization associated with the presence of degenerative disc disease, rules out other differentials causing bony lesions and assists with confirmation of anatomical landmarks. One study determined that in-situ disc mineralization in the thoracolumbar spine of Dachshunds at 2 years of age was a significant predictor of future clinical disc herniation. Survey radiography, however, lacks accuracy in identifying the exact location of the extruded disc. Accuracy for determining the site of thoracolumbar intervertebral disc extrusion using survey radiography ranged from 51–61 % in one study. Roentgen findings of suspected disc extrusion (**318**) include the following:

- Narrowing of the disc space.
- Altered shape of the intervertebral foramen.
- Wedging of the disc space.
- Presence of mineralized material in the vertebral canal or superimposed over the intervertebral foramen.

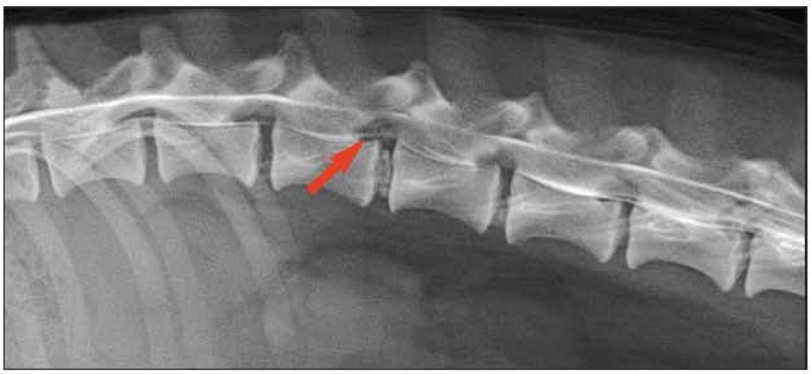


▲ 318 Lateral radiograph of the thoracolumbar junction demonstrating radiographic signs of intervertebral disc disease. There is presence of in-situ mineralization (red arrows) at T10/T11, T13/L1 and L1/L2. The intervertebral disc space at T11/T12 is wedged (yellow arrows) and the space between the articular processes is collapsed (black arrow), which is suggestive for the site of the disc extrusion.

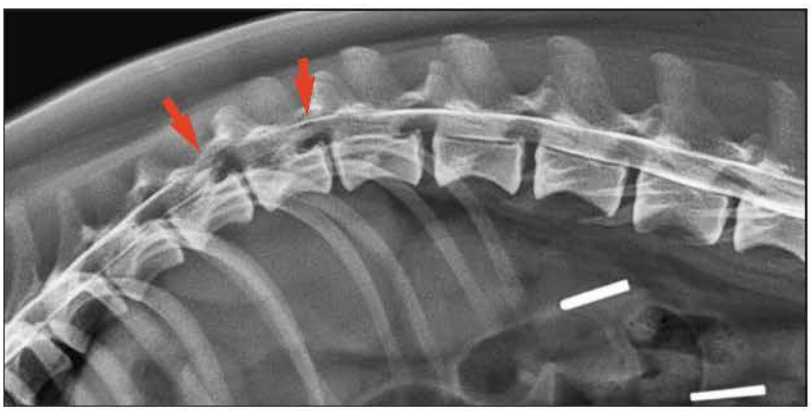
Myelography

Myelography has served as a standard for diagnosing spinal cord compression in dogs with IVDD. A non-ionic, radiographic contrast medium is injected into the subarachnoid space at the cerebellomedullary cistern or caudal lumbar (L4/L5, L5/L6) region. Attenuation of contrast flow within the subarachnoid space occurs at sites of compression and subarachnoid space occlusion; such patterns are described as extradural, intradural extramedullary and intramedullary (**319**). Lateral, ventrodorsal and oblique views are useful for determining the circumferential and longitudinal location and extent of the extradural compression. Longitudinal lesion localization by myelography in thoracolumbar IVDD has nearly 90% accuracy. An intramedullary pattern associated with spinal cord oedema is more common with acute extrusions and may obscure the site of extradural compression (**320**). Extensive longitudinal subarachnoid space attenuation of contrast flow can be seen with haemorrhage and/or spinal cord swelling. The extent of spinal cord swelling seen with myelography may assist in establishing a prognosis. Dogs with absent nociception have a significantly worse outcome if the extent of spinal cord swelling is greater than five times the length of L2. Myelomalacia is suspected when there is leakage of contrast medium into the spinal cord parenchyma during myelography.

Common technical problems associated with myelography include difficulties during injection and poor distribution of contrast medium. Anatomical problems include atypical displacement of disc material and the presence of spinal cord swelling. Systemic complications of myelography include seizures, worsening of neurological status, apnea, cardiac arrhythmias, meningitis, subarachnoid haemorrhage and death.

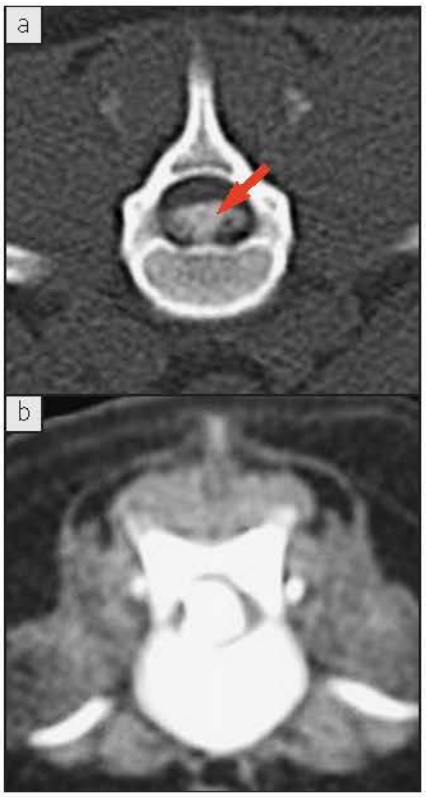


◀ **319** Lateral radiograph of the caudal thoracic and lumbar spine after injection of contrast medium. There is an extradural myelographic pattern (arrow) at L2/L3 characterized by dorsal deviation of the ventral contrast column caused by Hansen type I intervertebral disc disease.

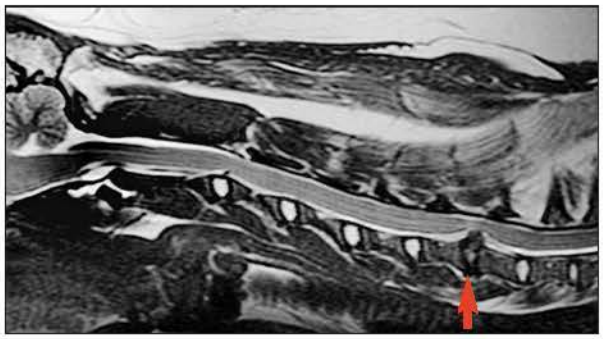


◀ **320** Lateral radiograph of the thoracolumbar spine after injection of contrast medium. There is an intramedullary pattern (arrows) extending from T12/T13 to L1/L2 and obscuring the site of extradural compression.

▶ **321** Transverse CT images. (a) An acute disc extrusion over the body of T13 demonstrating heterogeneous attenuation (arrow). (b) A chronic disc extrusion over the body of L1 demonstrating homogeneous attenuation.



▼ **322** T2-weighted mid-sagittal image of the cervical spine. Hansen type I disc degeneration, recognized by loss of signal intensity within the nucleus pulposus (arrow), can be seen at C6/C7. Notice also the area of extruded disc causing ventral spinal cord compression.

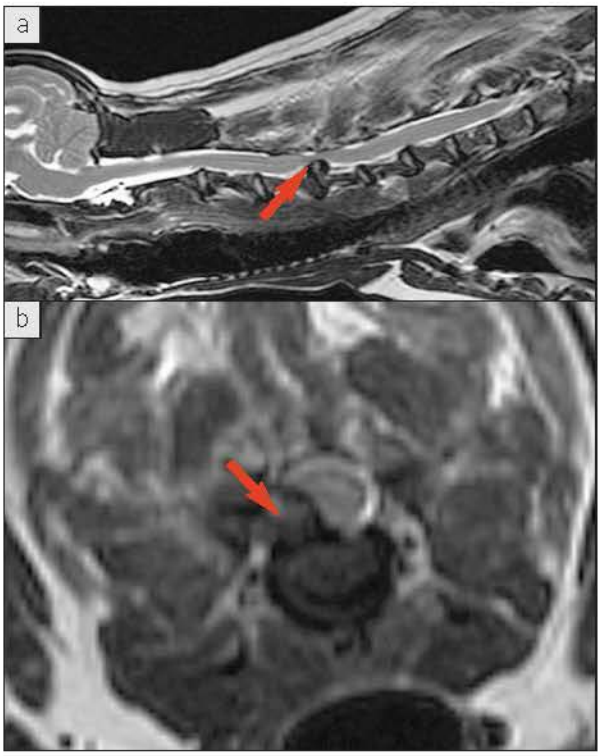


Computed tomography

CT is an adjunctive procedure to myelography to further delineate lateralization of the extruded disc material or it can be used as the sole technique for detecting intervertebral disc extrusion. Imaging the spine using CT alone is non-invasive and performed more quickly and with fewer complications than myelography. The lesion extent and lateralization of disc material are more distinct on CT than with myelography. Mineralized disc material and acute haemorrhage can be identified in the vertebral canal using non-contrast-enhanced CT. Acutely extruded disc material typically is recognized as a heterogeneous hyperattenuating extradural mass (**321**). The attenuation of the disc material increases with the degree of mineralization. Chronically extruded disc material has a more homogeneous hyperattenuating appearance. If more than one site has extruded disc material, a myelogram may be necessary to identify the site of the lesion based on a corresponding area of cord swelling. A more chronic lesion often will not have associated spinal cord swelling. Spinal cord swelling or oedema may also be identified using MRI based on identification of an area of high signal intensity on T2-weighted images associated with disc compression.

Magnetic resonance imaging

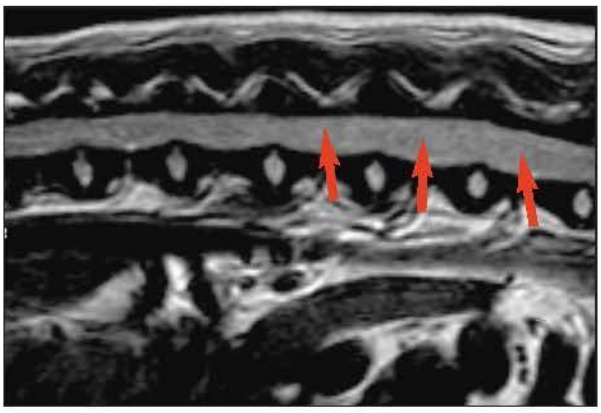
MRI is superior in the recognition of intraparenchymal pathology and has become the standard for the assessment of acute spinal cord injury in human patients. Standardized MRI protocols for intervertebral disc disease often use T1- and T2-weighted sagittal and transverse (axial) images over the areas of interest. MRI also is considered the best method for early recognition of in-situ disc degeneration based on a decrease in signal intensity within the nucleus pulposus on T2-weighted images (**322**). The hypointensity seen with degenerative disc disease is linked with changes in proteoglycan concentrations. Focal signal void within the intervertebral disc



▲ **323** T2-weighted MR images of an extruded disc at C4/C5. (a) Sagittal image with signal void suggestive of mineralization causing ventral spinal cord compression (arrow). (b) Transverse image of the same disc as in 323a with areas of signal void of the extruded disc material (arrow) right of midline and displacing the spinal cord to the left. Note the hyperintensity in the spinal cord from presumptive oedema.

space or vertebral canal may represent a free fragment of mineralized nucleus pulposus (**323**). Acute pathologies of spinal cord tissue seen as high signal intensity on T2-weighted images include necrosis, myelomalacia, intramedullary haemorrhage, inflammation and oedema. However, it is difficult to distinguish between these specific types of pathology. Areas of focal high signal intensity on T2-weighted images in chronic spinal cord disease are suggestive of focal myelomalacia and syringohydromyelia. MRI studies of myelomalacia in dogs with intervertebral disc extrusion and acute-onset paraplegia have demonstrated parenchymal high signal intensity on T2-weighted images and diffuse hypointensity on gradient echo images, cranial and caudal to the compressive extradural lesion (**324**).

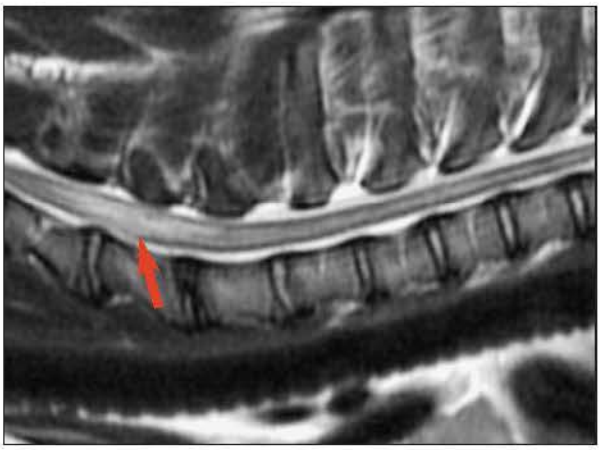
MRI may provide better clarity than other imaging techniques in detecting haemorrhage associated with intervertebral disc extrusion. However, timing of MRI in relation to onset of the lesion can confound the interpretation of signal intensity since rapid changes can occur within areas of haemorrhage in the early stages after injury. The presence of an extradural mass of low signal intensity on T1- and T2-weighted images near the mineralized disc material may be suggestive of recent haemorrhage or haematoma (**325**). A haematoma that is hours to several days of age typically appears hypointense on T2-weighted and gradient echo images until conversion of deoxyhaemoglobin to methaemoglobin. Intracellular methaemoglobin causes pronounced shortening of the T1 relaxation times of tissues because its paramagnetic properties alter proton interactions.



◀ **324** T2-weighted sagittal thoracolumbar MR image demonstrating homogeneous hyperintensity within the swollen lumbar spinal cord (arrows) becoming more heterogeneous towards the unaffected thoracic spinal cord. This dog demonstrated clinical and pathological features of myelomalacia.



▲ 325 T2-weighted transverse MR image of the thoracolumbar spine at the T12/T13 disc space. A large extradural mass of low signal intensity is present (arrow) lateral to the spinal cord. Note that the spinal cord is displaced. Surgery confirmed that the low signal was epidural haemorrhage.



▲ 326 Sagittal T2-weighted MR image of the cervicothoracic spine demonstrating extensive intramedullary swelling and hyperintensity (arrow) from C5–C7 associated with a traumatic non-compressive disc extrusion.

Thus methaemoglobin appears hyperintense on T1-weighted images. The presence of deoxyhaemoglobin does not cause T1 shortening and appears isointense to the spinal cord on T1-weighted images.

MRI has been used to predict prognosis in paraplegic dogs caused by intervertebral disc extrusion. Results suggest that dogs with an area of hyperintensity at least as long as the L2 vertebral body seen on pre-operative T2-weighted sagittal MR images of the spinal cord have a poorer prognosis for functional recovery (**326**). The success rate following surgery in dogs without hyperintensity of the spinal cord was 100% compared to 55% in those with areas of hyperintensity. Moreover, the success rate reported for dogs with areas of hyperintensity and loss of nociception was 31%, and the success rate in dogs with no nociception and hyperintensity >3 times the length of the L2 vertebral body was 10% (1/10 dogs). As expected, the degree of cord compression noted on MRI of thoracolumbar disc disease has not been associated with prognosis.

Cerebrospinal fluid analysis

CSF analysis is unlikely to confirm a diagnosis of IVDD, but may help to rule out primary inflammatory CNS disease. Moderate to marked lymphocytic CSF pleocytosis (>5 cells/μl) is seen in dogs with Hansen type I IVDD, especially in those with chronic presentation or in an acute presentation of chronic IVDD. Protein concentration elevations have been associated with acute-onset disease and clinical severity. Albuminocytological dissociation is also a common clinicopathological finding in IVDD.

MANAGEMENT

Medical management

Indications for medical management of IVDD include first time incidence of spinal pain only, mild to moderate paresis and financial constraints of the pet owner. In general, conservative therapy consists of pain control and strict cage rest. Strict cage confinement enforced for a minimum of 4–6 weeks is an essential aspect of successful conservative management.

General concepts

Dogs with initial pain or minimal motor dysfunction can be managed by strict cage rest for 4–6 weeks combined with pain management using anti-inflammatory drugs (NSAIDS, opioids and muscle relaxants). The importance of cage rest is that it allows for annular and ligamentous healing and prevention of further disc herniation. Fluid therapy is important at the time of the injury in order to maintain spinal cord perfusion. MPSS (30 mg/kg IV slow bolus) administered within the first 8 hours from onset of trauma has been advocated as an adjunctive treatment of acute disc herniation causing paraplegia and loss of nociception. Dexamethasone (0.5–1.0 mg/kg IV once) or prednisone (0.5–1.0 mg/kg PO q12–24h for 5 days, then taper) has also been advocated to reduce spinal cord oedema. However, administration of corticosteroids is controversial from the standpoint of countering pathophysiological mechanisms and efficacy still remains to be proven. Corticosteroid use in dogs with acute IVDD can increase rates of postoperative complications (which include gastrointestinal disease) and financial cost to the client. NSAIDs should not be used in combination with corticosteroids as gastric ulceration and potentially fatal perforation can result. Gastrointestinal protection may be necessary if anti-inflammatory therapies are used. Dogs treated conservatively should be assessed daily for pain level, comfort, bladder emptying, evidence of decubital ulceration and neurological status. Acupuncture and muscle relaxants have also been advocated as treatments for pain management. Cases with recurrent episodes of neck or back pain uncontrolled by medication and/or worsening of neurological status should have decompressive surgery. Physical therapy, weight control and avoidance of jumping activities may reduce recurrence rates.

See Chapter 21 for more information on the treatment of spinal injury and Chapter 30 for a more detailed discussion of patient analgesia.

Cervical intervertebral disc disease

Conservative therapy can be attempted while the dog is monitored for reduction of pain and improvement in neurological status. In dogs with cervical IVDD, conservative therapy alone is often ineffective. A possible reason for lack of response to strict cage rest is that total immobility of the cervical spine is difficult to maintain. Additionally, dogs with cervical spinal pain as the primary presenting sign may have a significant amount of extruded disc present within the spinal canal.

In the author's experience, surgical management is recommended when pain is refractory to standard pain management for longer than 1–2 weeks or if there is progression of neurological deficits. There is limited information available on the success of medical therapy for cervical IVDD in dogs, but the recurrence rate has been reported to be as high as 36%. More recently, a success rate of nearly 50% has been reported, with 33% having recurrence of clinical signs and 18% having therapeutic failure. This study also suggested that duration of cage rest was not significantly associated with success or 'quality of life' scores. It was stated that an initial period of strict cage confinement may be beneficial, but that prolonged (>2 weeks) strict rest at the expense of physical rehabilitation may not have any benefit.

Thoracolumbar intervertebral disc disease

Indications for medical treatment of dogs with thoracolumbar IVDD include first time incidence of spinal pain only, mild to moderate non-progressive paraparesis and financial constraint of the client.

Success rates for conservative management of ambulatory dogs with thoracolumbar pain only and/or mild paresis range from 82–100%. Recovery rates in non-ambulatory dogs with thoracolumbar disease are lower and recurrence rates are higher in studies following conservative treatment. More recent retrospective studies of conservatively managed dogs with thoracolumbar disc disease documented 30–50% recurrence rates in dogs with minimally affected ambulatory status. Recurrence of spinal hyperpathia in dogs with thoracolumbar IVDD that are conservatively managed usually occurs within 6 months to 1 year from onset of the initial clinical signs.

Surgical management

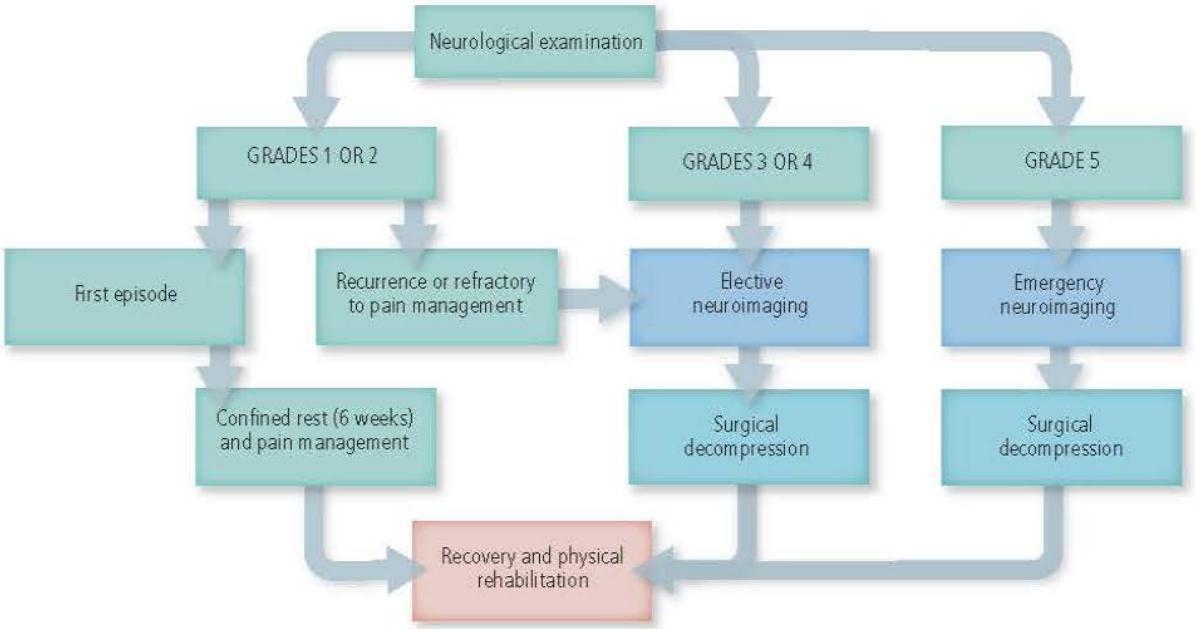
Decisions for emergency surgery in dogs with acute IVDD should take into account the severity of the neurological status, the rapidity of deteriorating neurological signs and the patient's overall health status. Patients presenting with plegia and absent nociception need emergency surgical decompression (**327**).

Goals for surgical management of dogs with spinal cord injury include decompression, removal of extruded disc and haemorrhage, and visual observation of the spinal cord. Chronicity of disc extrusion at the time of surgery may influence the ease with which extruded disc material can be removed. Decompressive procedures for IVDD include ventral slot, dorsal laminectomy, hemilaminectomy, partial corpectomy and pediculectomy (also termed mini-hemilaminectomy). The primary purpose of decompressive surgery is to allow for adequate exposure for removal of disc material while minimizing spinal cord manipulation. There are advantages and disadvantages of each decompressive technique.

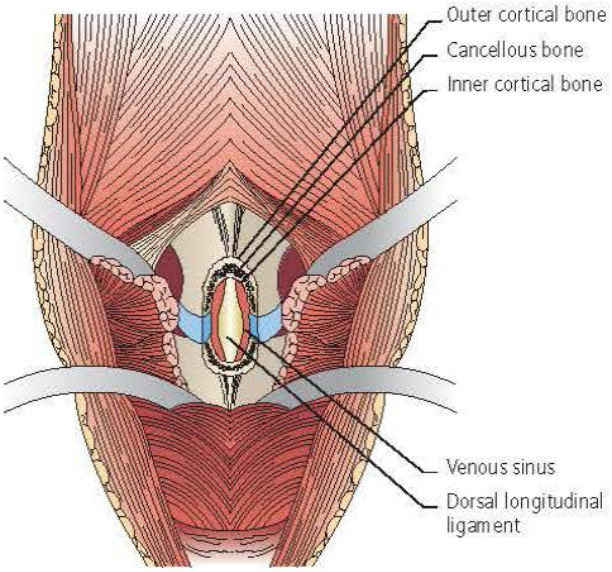
Cervical intervertebral disc disease

Indications for surgical treatment of cervical intervertebral disc extrusion include pain refractory to medical management and/or severe and progressive neurological deficits.

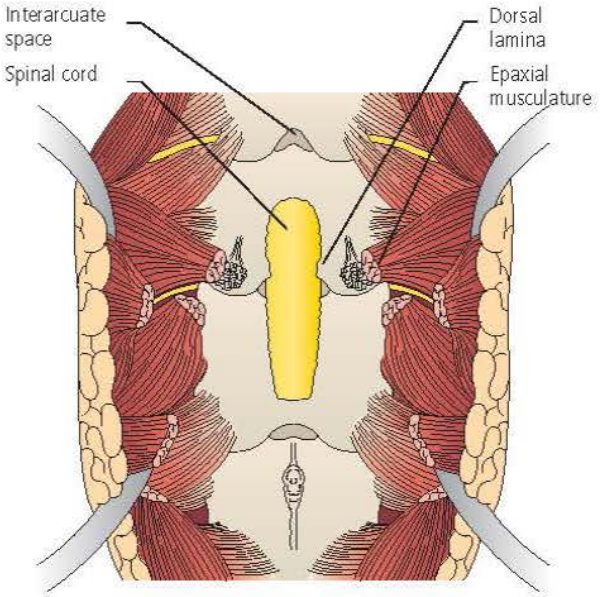
In cervical IVDD, decompressive procedures via a ventral, lateral or dorsal approach are the techniques of choice for removal of extruded disc. The selection of the decompressive procedure is usually determined by the



▲ **327** **Decision-making algorithm with respect to the surgical management of a dog with thoracolumbar disc herniation.**



▲ 328 Ventral slot procedure after drilling. The slot is more extensive in the vertebra cranial to the disc. Drilling depth is judged by recognition of the outer cortical bone, cancellous bone and inner cortical bone. Other structures not easily visualized are the paired venous sinuses and the dorsal longitudinal ligaments. (Adapted from Coates JR, Hoffman A, Dewey CW (2003) Surgical approaches to the spine. In: *Textbook of Small Animal Surgery*, 3rd edn. (ed. D Slatter) WB Saunders, Philadelphia, pp. 1148–1162.)



▲ 329 Dorsal laminectomy in the cervical spine: shown here is the epaxial musculature attached to articular process; the edge of the laminectomy defect; the interarcuate space; and the spinal cord. (Adapted from Coates JR, Hoffman A, Dewey CW (2003) Surgical approaches to the spine. In: *Textbook of Small Animal Surgery*, 3rd edn. (ed. D Slatter) WB Saunders, Philadelphia, pp. 1148–1162.)

location of the disc material in relation to the cord. The ventral slot technique is commonly performed for disc displaced ventral to the spinal cord (**328**). Using the identifiable landmarks of the ventral prominence of C1 and the transverse processes of C6 to identify the disc interspace of interest, a slot is cut into the ventral aspect of the cervical vertebrae using a high-speed surgical drill. Advantages of the ventral decompressive technique include minimal muscle dissection and exposure for prophylactic fenestration of adjacent cervical discs. Disadvantages may include excessive venous sinus haemorrhage, lack of spinal cord decompression and inadequate exposure for lateral or intraforaminal disc extrusion. If the width of the slot is >30% of the size of the vertebral body, dogs may suffer from instability or subluxation at the surgery site.

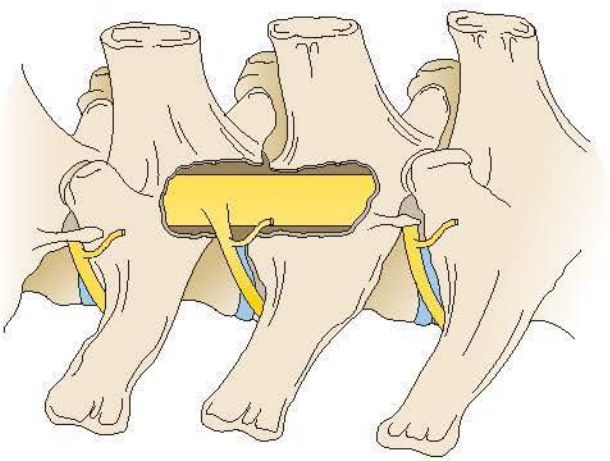
Dorsal laminectomy involves dissection of the epaxial musculature and removal of the dorsal spinous processes and the laminae (**329**). Dorsal procedures provide spinal cord decompression and access for laterally extruded disc material, but access is limited to extruded disc located beneath the spinal cord. A lateral approach has been described for lateral or intraforaminal disc extrusions at the C4/C5 and C5/C6 interspaces. Excessive haemorrhage from muscle dissection and damage to the internal vertebral venous plexus or vertebral artery and incomplete removal of disc material can be complications of dorsal decompression. The risk for spinal instability is considered less when compared with the ventral slot technique.

Thoracolumbar intervertebral disc disease

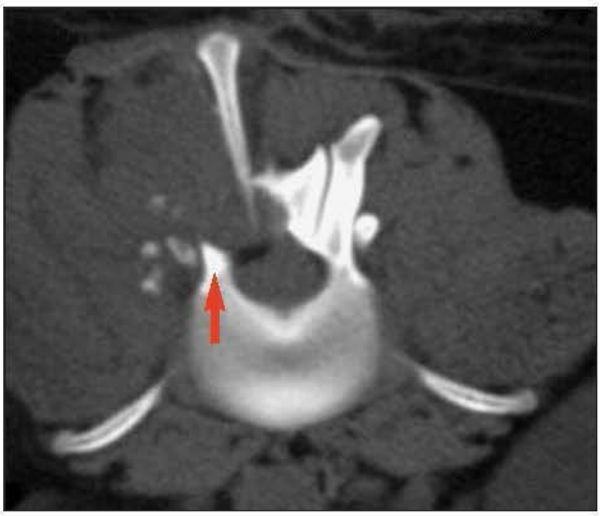
Indications for surgical management of thoracolumbar IVDD include spinal pain or paresis refractory to medical therapy, recurrence or progression of neurological deficits, paraplegia with intact nociception and paraplegia with loss of nociception for less than 24–48 hours. Prolonged loss of nociception (>48 hours) carries a poorer prognosis and owners should be made aware of this prior to surgery.

Decompressive procedures for thoracolumbar IVDD include dorsal laminectomy, hemilaminectomy and pediculectomy. Hemilaminectomy significantly improves retrieval of extruded disc material, with minimal spinal cord manipulation (**330**). Pediculectomy is the least invasive and least destabilizing technique and can be used as an adjunctive technique in cases requiring a bilateral approach to the vertebral canal. An accurate 3D depiction of the disc location is necessary prior to pursuing this surgical technique due to the small surgical field that it provides. Biomechanical studies have shown that unilateral facetectomy and fenestration do not significantly destabilize the spine during lateral bending.

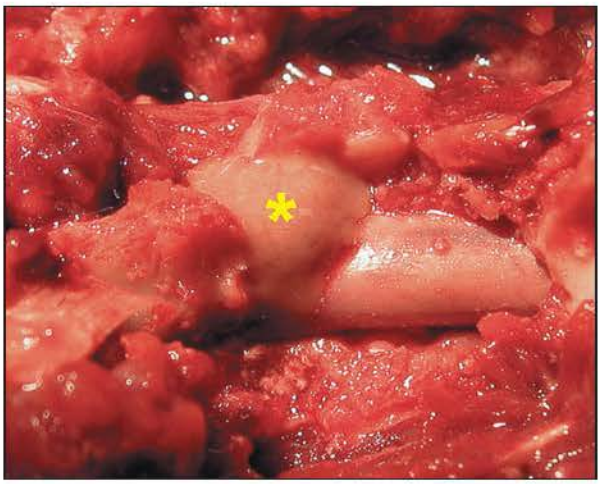
The type of decompressive procedure may not affect outcome; however, the ability to retrieve the disc material depends on the type of decompressive procedure selected. Hemilaminectomy provides the same degree of decompression as dorsal laminectomy and is less frequently associated with a postsurgical constrictive laminectomy membrane. Radical bilateral dorsal laminectomy (removal of pedicle – Funkquist A) has an increased risk of constrictive laminectomy membrane formation. Studies have reported retrieval of disc material in 93% of dogs that had hemilaminectomy compared with 40% of dogs that had dorsal laminectomy, but the initial neurological recovery after hemilaminectomy was not significantly different compared with dorsal laminectomy. Surgical complications include excessive haemorrhage, incomplete removal of extruded disc (**331**), constrictive fibrosis and, rarely, instability.



▲ **330** Location and extent of a typical left-sided hemilaminectomy. (Adapted from Coates JR, Hoffman A, Dewey CW (2003) Surgical approaches to the spine. In: *Textbook of Small Animal Surgery*, 3rd edn. (ed. D Slatter) WB Saunders, Philadelphia, pp. 1148–1162.)



▲ **331** Transverse CT image of an incomplete hemilaminectomy with pedicle (arrow) still remaining and preventing adequate visualization of the vertebral canal ventral to the spinal cord.



▲ **332** **Intraoperative photograph demonstrating myelomalacia (asterisk) after durotomy over the cranial aspect of the exposed spinal cord. (Photo courtesy Robert Bergman)**

If the patient has absent nociception prior to surgery, a durotomy can be considered for visualization of the spinal cord parenchyma to determine the extent of swelling and the presence of myelomalacia (**332**). However, durotomy is ineffective as a treatment for acute compressive spinal cord trauma caused by IVDD. Absence of visual evidence of myelomalacia does not guarantee functional recovery; conversely, recovery may still occur despite the presence of focal myelomalacia.

Although controversial, intervertebral disc fenestration has been advocated as a prophylactic procedure to prevent future extrusions at adjacent spaces. Prophylactic intervertebral disc fenestration was recommended after similar recurrences were noted in patients that underwent spinal decompression and those that were managed conservatively. Fenestration of the herniated disc at the time of spinal decompression is recommended to prevent continued extrusion of disc material. Surgical approaches for disc fenestration include dorsolateral, lateral and ventral. Power-assisted and manual methods have been described for disc fenestration. The effectiveness of fenestration is related to the amount of nucleus pulposus removed. Multiple disc fenestrations are performed from T11/T12 to L3/L4, sites more commonly predisposed to disc herniation. Reasons for not performing fenestration include surgical complications (which include extruding further disc), increased anaesthetic time and increased costs to the pet owner. Fenestration is not recommended in large non-chondrodystrophic dogs due to the potential for underlying spinal instability as a predisposing factor for annular protrusion.

Role of fenestration

Prophylactic fenestration typically is performed from T11/T12 to L3/L4. Published studies suggest recurrence rates of 0–24% with prophylactic fenestration and 2.7–42% without prophylactic fenestration. Dogs undergoing prophylactic fenestration tend to have lower recurrence rates. One study determined a 4.7% recurrence rate after multiple disc fenestrations in 265 dogs, but commented that prophylactic fenestration could promote disc extrusion at an adjacent non-fenestrated disc. These findings provide further support for additional therapeutic interventions such as prophylactic fenestration and disc ablative procedures.

PROGNOSIS

Cervical intervertebral disc disease

Prediction of recovery outcomes in dogs with cervical IVDD based on site of herniation, ambulatory status and breed size is controversial (*Table 86*). In a study of 190 dogs with cervical IVDD treated surgically, outcomes were no different for the ambulatory versus non-ambulatory dogs with intact nociception. After surgery, 99% of those dogs had resolution of cervical spinal hyperaesthesia and were able to ambulate unassisted. Other previous studies have reported that dogs with caudal cervical disc extrusions respond less favourably and are more severely affected than dogs with cranial cervical disc extrusions. A study that also included dogs with Hansen type II IVDD associated with caudal cervical spondylomyelopathy reported only a 66% success rate following surgery in large breed dogs. Recently, a study in 32 dogs with non-ambulatory tetraparesis reported that 62% had a complete recovery. Small dogs were 6 times more likely to recover than large breed dogs and dogs that regained the ability to walk within 96 hours after surgery were 7 times more likely to recover than those not ambulating within 96 hours. If given more

Table 86 **Reported recovery outcomes in dogs with cervical IVDD**

NEUROLOGICAL STATUS	SUCCESS OF MEDICAL MANAGEMENT	SUCCESS OF SURGICAL MANAGEMENT
Pain, mild paresis	50% (Levine *et al.*, 2007)	66% (large breed) (Chambers *et al.*, 1986) 87% (Fry *et al.*, 1991) 99% (Cherrone *et al.*, 2004)
Non-ambulatory tetraparesis	Unknown	62% (Hillman *et al.*, 2009)
Recurrence rate	33% (Levine *et al.*, 2007) 36% (Russell and Griffiths, 1968)	6% (Russell and Griffiths, 1968) 10% (8% small breed; 13% large breed) (Cherrone *et al.*, 2004) 33% (Toombs, 1992)

time, however, recovery of ambulatory function can occur, but residual deficits are likely. In contrast to previous studies, the site of disc herniation was not a significant predictor of complete recovery. Compared with thoracolumbar IVDD, the severity of neurological deficit was not a robust predictor of outcome.

Recurrence of clinical signs after surgery in dogs with cervical IVDD has been reported to range from 10–33% (*Table 86*). The most common clinical sign during recurrence was cervical spinal hyperaesthesia. A second disc extrusion at a site distinct from the initial lesion was the most common reason for recurrence.

Thoracolumbar intervertebral disc disease

Differences in recovery rates of non-ambulatory dogs with thoracolumbar IVDD vary with the severity of neurological dysfunction (neurological grade), time interval from initial clinical signs to surgery and speed of onset of signs (*Table 87*, pp. 414–415). Overall success rates after decompressive surgery range from 58.8–95%. However, the success of a surgical approach may depend on what criteria are used to define it and how long after the surgery the patient is assessed, as well as the outcome that the owners are willing to accept. In other words, surgical success may consist of improvement in the patient's neurological grade, but still may not translate to complete normality. It has been reported that approximately 40% of dogs that recovered from loss of nociception (grade 5) continued to have faecal incontinence. Additionally, recurrent urinary tract infection can occur in dogs recovering from non-ambulatory neurological status. Residual signs such as faecal and urinary incontinence can be unacceptable to some pet owners.

Dogs with thoracolumbar IVDD and ambulatory dysfunction will often have concomitant UMN urinary bladder dysfunction. These dogs will require manual bladder expression and intermittent or indwelling urinary bladder catheterization. Incomplete bladder evacuation and use of urinary catheters may predispose dogs to urinary tract infection (UTI). A prospective study in dogs with thoracolumbar IVDD determined that the prevalence of UTI was 30%, with a higher incidence in dogs that were female and had lower intraoperative body temperatures. However, intermittent urinary catheterization has a lower risk of inducing a UTI over indwelling closed-system urinary catheterization techniques. If an indwelling system is selected, minimizing the duration of use is important for reducing the risk of UTI.

Table 87 **Reported recovery outcomes in dogs with thoracolumbar IVDD**

NEUROLOGICAL STATUS	SUCCESS OF MEDICAL MANAGEMENT	SUCCESS OF SURGICAL MANAGEMENT
Pain, ataxia, paraparesis	75–85% (Hoerlein, 1978; Funkquist, 1978; Davies and Sharp, 1983); 55% (Levine *et al.*, 2007)	>95% (Davies and Sharp, 1983; Forterre *et al.*, 2008); 96% (pain only) (Sukhiani, 1996); 96% (Schulman and Lippincott, 1987); 65–83% (Brown *et al.*, 1977)
Paraplegia with superficial nociception	51% (Funkquist, 1970)	79% (Schulman and Lippincott, 1987); 81% (Funkquist, 1970); 82% (Ruddle *et al.*, 2006); 86% (Forterre *et al.*, 2008); 91% (Brisson *et al.*, 2004); 96% (Davies and Sharp, 1983)
Paraplegia with deep nociception	50% (Davies, 1983)	86% (Ferrira, 2002); 89% (Gambaredella, 1980)
Absent deep nociception <12 hours	5–10% (Davies, 1983)	47% (Brown *et al.*, 1977); 50% (Gambaredella, 1980); 58% (Olby *et al.*, 2003); 60% (Loughin *et al.*, 2005); 62% (Scott, 1997); 69% (Ruddle *et al.*, 2006); 76% (Anderson *et al.*, 1992)
Absent deep nociception >48 hours	5–10% (Davies, 1983)	6.7% (Loughin *et al.*, 2005); 33% (Scott and McKee, 1999)

(Continued)

In general, dogs with more severe motor dysfunction tend to have longer recovery times for regaining ambulatory function. Reported mean time from surgery to a pain-free ambulatory status varies from 10 days for dogs presenting with spinal pain only to 52 days for paraplegic dogs. Other long-term studies reported the recovery times as 2–14 days for dogs that were either ambulatory or nonambulatory paraparetic and up to 4 weeks for paraplegic dogs. In a recent report on 218 nonambulatory dogs with intact nociception, 42% were ambulatory by 2 weeks and 79% ambulatory by 4 weeks following decompression. This same study also reported that dogs with disc extrusions caudal to L3–L4 are likely to achieve ambulatory status sooner than dogs with disc extrusions between T10 and L3. Patient age and weight also have an association with the time required for ability to ambulate. Moreover, dogs that undergo physical rehabilitation may have shorter times to return of ambulation.

There are many contradictory studies on the effect of rate of onset and duration of signs prior to surgery on speed of recovery and final outcome. It is agreed that rapid removal of extruded disc material facilitates a more complete and rapid recovery. Dogs with shorter duration of signs and gradual onset of neurological dysfunction (<48 hours) have a quicker recovery. However, a study of 71 paraplegic dogs with intact nociception demonstrated that although a shorter duration of signs was indeed associated with a shorter recovery time, the rate of onset of clinical signs did not influence the recovery time, but it

Table 87 **Reported recovery outcomes in dogs with thoracolumbar IVDD** *(continued)*

NEUROLOGICAL STATUS	SUCCESS OF MEDICAL MANAGEMENT	SUCCESS OF SURGICAL MANAGEMENT
Recurrence rate	48% (Funkquist, 1978); 34% (Davies, 1983); 40% (Levine, 1984); 33% (Ferreira, 2002); 50% (Mann, 2007)	**Without fenestration:** 3% (Brown *et al.*, 1977); 5% (Muir, 1995); 6% (Dhupa *et al.*, 1999); 6% (Olby *et al.*, 2003); 15% (Necas, 1999); 16% (Brisson *et al.*, 2004); 19% (Mayhew *et al.*, 2004); 23% (Black, 1988); 27% (Levine and Caywood, 1984); 17% (Funkquist, 1978); 32% (McKee, 1992); 42% (Funkquist, 1970) **With single site fenestration:** 15% (Ferreira, 2002); 13% (Scott, 1997) **With multi-site fenestration:** 0% (Black, 1988); 4% (McKee, 1992); 4.4% (Brisson *et al.*, 2004); 3.5% (Bartels, 2003); 6.25% (Olby *et al.*, 2003); 16% (Levine and Caywood, 1984); 24% (Knapp, 1990)

did influence the final outcome. Similarly, peracute onset of signs indicated a poorer prognosis for dogs with no nociception. One study compared the outcome of dogs after hemilaminectomy with duration of clinical signs and concluded that delay before surgery does not influence outcome in dogs with mild neurological dysfunction, but does affect better functional recovery in paraplegic dogs when performed within 12 hours.

Nociception is considered the most important prognostic indicator for functional recovery. In general, the majority of dogs with intact nociception, whether paraplegic or paraparetic, have an excellent prognosis, particularly if treated surgically. Without surgery, or with delayed surgery, dogs with absent nociception have an extremely guarded prognosis, although duration of absence of nociception prior to surgery as a prognostic indicator is controversial. In general, dogs with loss of nociception for longer than 24–48 hours prior to surgery have a poorer prognosis for return of function. Recovery rates for dogs with thoracolumbar IVDD and absent nociception range from 0–76%. Recovery of nociception within 2 weeks after surgery has been associated with a successful outcome to ambulatory status. In a study of 87 dogs with loss of nociception, 58% regained nociception and the ability to walk. In summary, dogs with absent nociception that have surgery within 12 hours have a better chance of more rapid and complete recovery than those with delay of surgery. The prognosis is considered poor if nociception does not return within 2–4 weeks after surgery.

Recurrence of clinical signs after decompressive surgery in dogs with thoracolumbar IVDD is a common clinical entity, with incidence rates reported from 2–42% (*Table 87*). Risk factors determined for recurrence include presence of radiographic mineralization of multiple discs at the time of first surgery (5–6 opacified discs = 50% risk) and if the breed is a Dachshund. The time for recurrence is usually between 1 month and 2 years after surgery. Early recurrence clinical signs within 1 month after surgery are probably related to residual compression at the original disc site; recurrence more than 1 month after surgery is usually caused by a disc herniation at a site distinct from the initial lesion. The prognosis for functional recovery is not affected by a second surgery. Subclinical recurrence noted on MRI is reported to be as high as 60% in dogs after thoracolumbar decompression.

FELINE INTERVERTEBRAL DISC DISEASE

Intervertebral disc disease in cats occurs less frequently than in dogs, with a reported incidence of 0.02–0.12%. Hansen type I IVDD usually occurs in middle-aged cats, with a mean age reported as 9 years and ranging between 1.5 and 17 years. Cats with lumbosacral IVDD are often older, with a mean age of 12 years. Rarely, intervertebral disc extrusions have been reported in cats younger than 5 years of age. Postmortem studies have shown that Hansen type II IVDD is a common incidental age-related change in older cats. The cervical spinal region has been reported as the most common site for disc protrusion followed by the mid to caudal lumbar region.

The onset of type I IVDD in cats is usually acute. Clinical signs of thoracolumbar IVDD include paraspinal hyperaesthesia, paraparesis/plegia and incontinence. Commonly reported signs for lumbosacral IVDD are reluctance to jump, low tail carriage, paraparesis, urinary incontinence and constipation.

Lesions of Hansen type I herniations occur most commonly in the thoracolumbar region, with a predilection to the caudal lumbar and lumbosacral regions. The more frequently reported sites were between the T11/T12 and L1/L2 disc spaces and at the L4/L5 disc interspace. Cats have tendencies to jump while applying increased biomechanical loads on their lumbar spine, which may predispose to caudal lumbar disc extrusions.

Similar techniques for diagnosis of spinal cord disease in dogs also apply for use in cats. Treatment includes both conservative and surgical methods based on neurological status. Cats do not seem to respond as well to conservative treatments. In cats, decompressive surgical techniques allow for a more rapid and complete clinical recovery and a definitive diagnosis. The long-term prognosis is considered good to excellent in the majority of cases.

STATUS EPILEPTICUS

Allison Haley & Simon Platt

INTRODUCTION

An epileptic seizure is defined as excessive and/or hypersynchronous neuronal electrical activity in the cerebral cortex resulting in paroxysmal episodes of abnormal consciousness, motor activity, sensory input and/or autonomic function. Essentially, seizure activity represents temporary abnormal forebrain function with clinical characteristics dependent on the location of the abnormality (see also Chapter 7). Status epilepticus (SE) is defined as continuous seizure activity lasting 20–30 minutes or longer. A clinically more practical definition would be a seizure lasting longer than 5 minutes, or two or more seizures between which the patient does not completely recover consciousness. Cluster seizures are defined as two or more seizures over a short period of time (minutes to 24 hours), between which the patient regains consciousness.

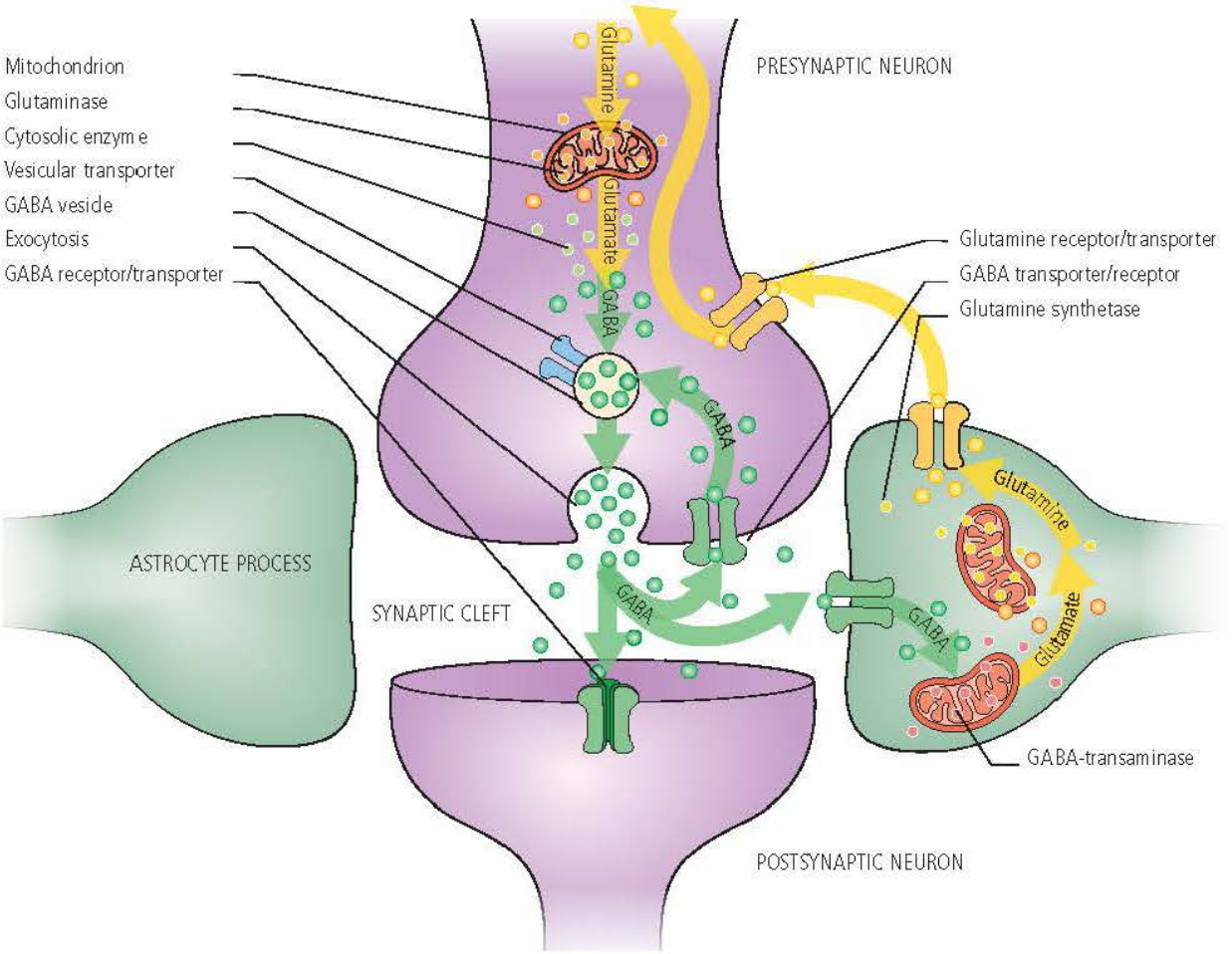
AETIOLOGY/PATHOPHYSIOLOGY

Seizure pathophysiology

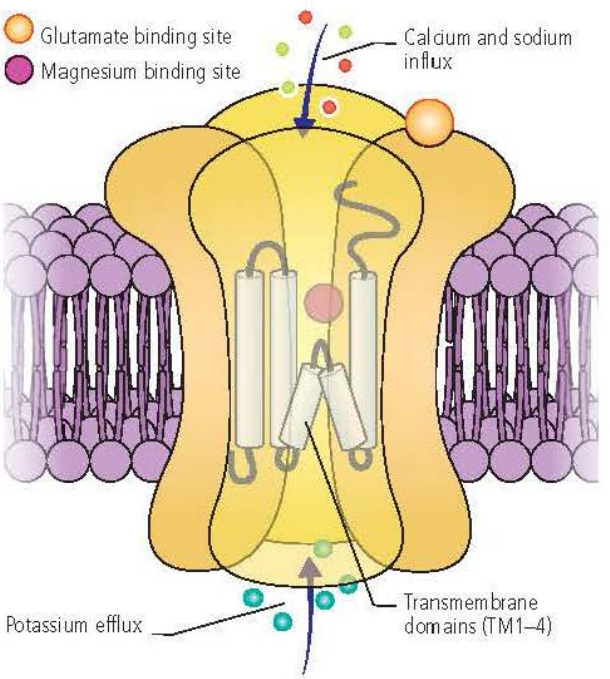
In normal neurons, like other cells, an action potential is created by changes in the cell membrane potential. The membrane potential is governed by the influx and efflux of ions through voltage-gated channels. At resting membrane potential the extracellular sodium concentration is much higher than the intracellular concentration. Distribution of potassium is just the opposite, with higher concentrations within the cell. An increase in the membrane's permeability to sodium results in depolarization. As the action potential reaches an axon terminal, the influx of sodium into the cell results in opening of calcium channels (see **125**, page 159). Calcium enters the cell and causes release of the neurotransmitter. Many neurotransmitters have been identified within the CNS. L-glutamate is an excitatory amino acid found in elevated concentrations when associated with seizure activity. GABA is the major inhibitory neurotransmitter of the CNS (**333**, next page and **126**, page 160). It is believed that altered GABAergic function is a major part of seizure pathophysiology.

At the time of a seizure there is an extracellular elevation in potassium and decrease in calcium, which is responsible for enhancing neuronal excitability and facilitating the spread of the seizure. If there is synchronization of the seizure discharge with other neurons, it may propagate to other areas of the brain. It is hypothesized that a population of cortical neurons within an epileptic focus undergo paroxysmal synchronous depolarization termed a paroxysmal depolarizing shift (PDS). This results in an abnormal burst of action potentials that continue in synchronous volleys without appropriate inhibition. Although elevated extracellular potassium levels may induce seizures, the occurrence of seizures is also dependent on intact synaptic inputs from the hippocampus, which appears to facilitate the transition from normal to ictal cell firing.

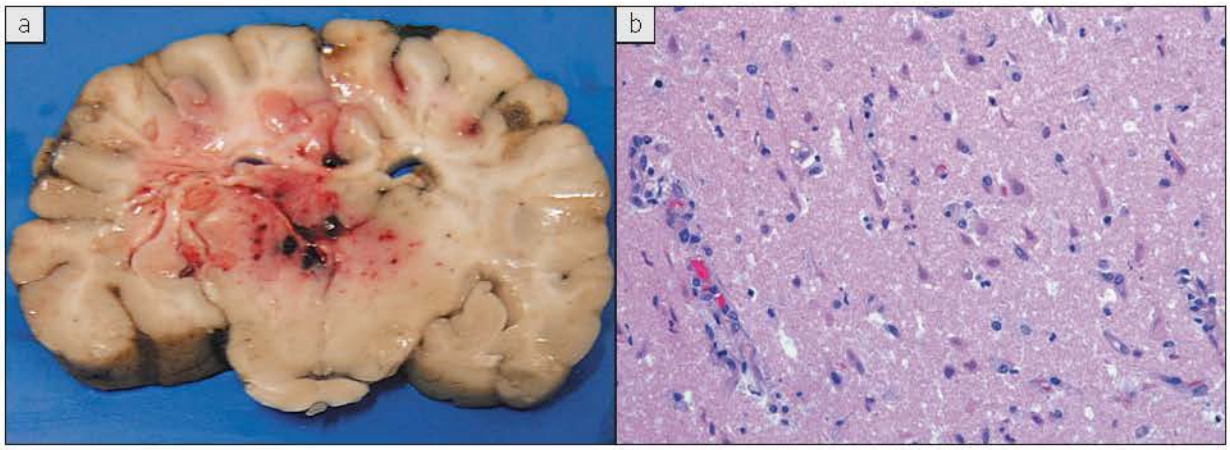
The basic pathophysiology of SE involves a failure of mechanisms that usually stop an isolated seizure. This failure can arise from abnormal excessive excitation or ineffective recruitment of inhibition. It is likely that numerous mechanisms are involved depending on the underlying cause. Recent experimental work has suggested that the failure of inhibition may be caused by a shift in the functional properties of the GABA receptor that occurs as seizures become prolonged. Repetitive neuronal firing imposes a massive metabolic demand, which is exacerbated by glutamate-mediated excitotoxicity and decreased GABA inhibitory neurotransmission. This has become known as the excitotoxic theory of neuronal damage.



▲ 333 **GABA is formed by alpha-decarboxylation of glutamate, a reaction catalysed by a cytosolic enzyme (L-glutamic acid-1-decarboxylase). GABA is taken up into storage vesicles, then released into the synaptic cleft by exocytosis. It is also taken up into the glia via GABA transporters where it is converted into glutamate by the mitochondrial enzyme GABA transaminase.**



▶ 334 **The N-methyl-D-aspartate (NMDA) receptor is an ionotropic glutamate receptor, which is distributed widely in the CNS. Each NMDA receptor consists of 4 transmembrane domains (TM1–TM4). The TM2 domain forms a kink, which serves as a gate and does not fully traverse the membrane. Magnesium binds to the receptor at normal resting potentials or when the cell is hyperpolarized, and blocks the NMDA receptor channel. When the cell is depolarized, the magnesium is dislodged, allowing sodium and calcium to enter the cell and potassium to leave.**



▲ 335 (a) Gross brain section of a dog with idiopathic epilepsy that experienced protracted status epilepticus unresponsive to medication. Note the haemorrhagic oedema and associated swelling, which resulted in cerebral herniation. (b) Histopathological section of thalamic grey matter in a dog that died following seizure activity. Multiple neurons are shrunken, angular and hypereosinophilic. These microscopic changes indicate acute neuronal degeneration and necrosis. These changes can occur as a result of seizure or ischaemic episodes. (Photo courtesy Raquel Rech)

Many molecular signals are triggered by SE, activating receptors in neuronal membranes. Activation of the NMDA receptor (**334**) has been shown to play a key role in neuronal signalling and delayed neuronal death. It has been shown that NMDA receptors become activated during continuous neuronal stimulation, and in several animal models, NMDA receptor antagonists have been shown to block or delay seizure activity. However, little is known about the receptor's precise role. Excessive concentrations of the excitatory amino acid glutamate cause NMDA receptors to open cation channels to calcium. Large amounts of calcium enter the neuron and then induce a cascade of intracellular neurochemical events that can kill the cells. Other possible neurotoxic substances released during SE include aspartate, free fatty acids, arachidonic acid and free radicals.

Certain areas of the brain are more sensitive to the detrimental effects of SE. The underlying biochemical reason for this increase in sensitivity is complex and not fully understood. One theory is that there is a mechanism mediated through glutamate's interaction with NMDA receptors. Administration of exogenous glutamate results in a similar distribution of neuronal damage as that of seizure-induced damage. The areas sensitive to neuronal necrosis in SE include the pyramidal cells of the hippocampus and the amygdala. Both these regions are rich in GABA, the major inhibitory neurotransmitter of the brain, therefore destruction of these regions predisposes the animal to future episodes of SE and can make long-term seizure control difficult.

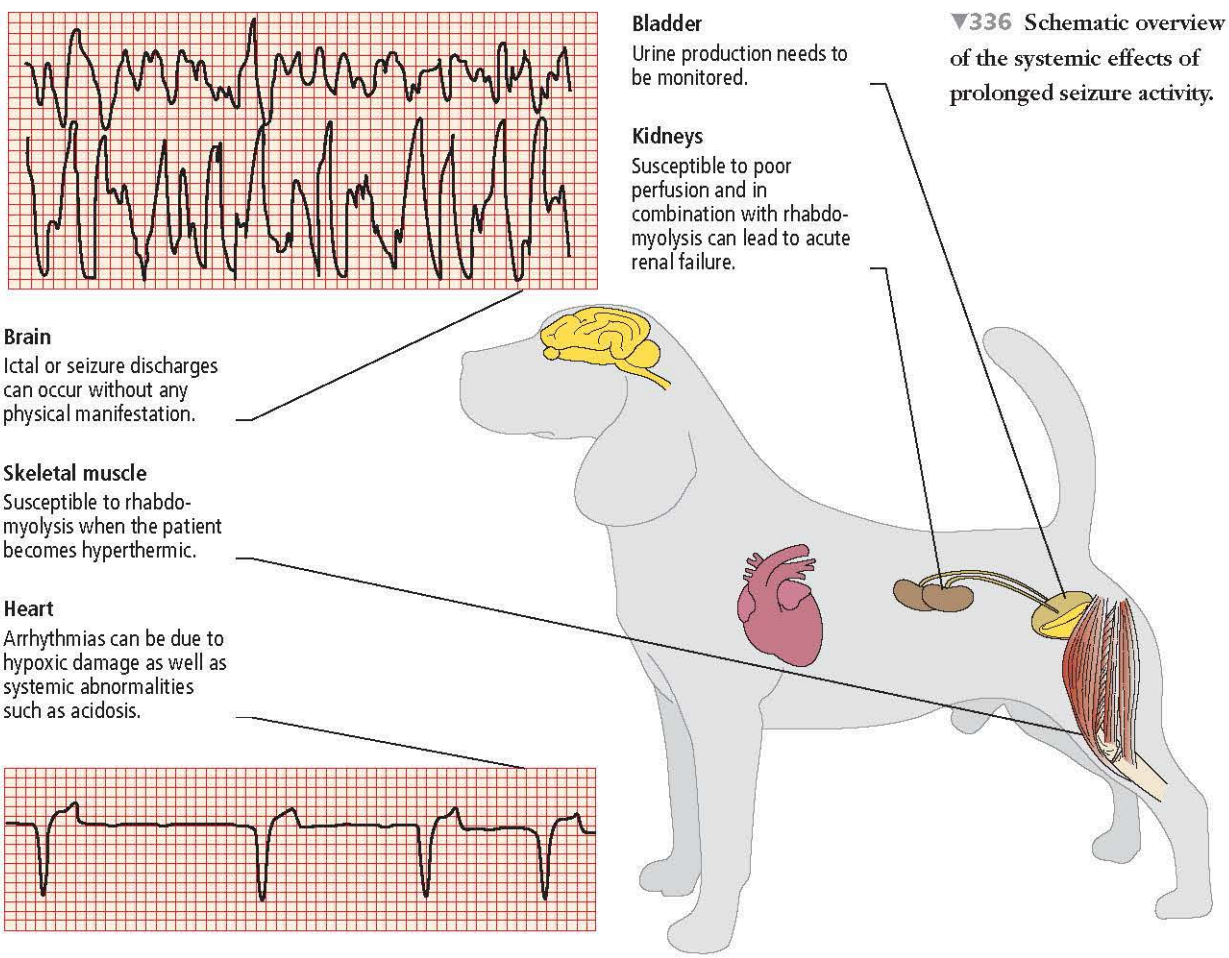
Brain injury, during prolonged seizure events, may also relate to a mismatch between substrate demand and supply. Compensatory factors may be unable to meet the considerable metabolic demand placed on the brain during seizures. SE lasting longer than 30 minutes can cause brain damage, especially in the limbic structures. In several animal models of SE, histopathological evidence of neuronal damage was identified within CA1 and CA3 sectors of the hippocampus; layers 3, 5 and 6 of the neocortex; Purkinje cells within the cerebellum; the thalamus; and the amygdala following prolonged seizure activity (**335**). Animal models have also demonstrated the deleterious role that hyperthermia, hypoxia and hypotension play in creating further neuronal damage. However, observation of neuronal changes in well-ventilated animals in which adequate glucose levels have been maintained suggests that ongoing seizure activity itself substantially contributes to neuronal damage.

Systemic consequences

SE can be divided into an early phase (0–30 minutes) and a late phase (beyond 30 minutes) based on the pathophysiological changes occurring.

The body's initial response to seizure activity is a release of large amounts of catecholamines, resulting in cardiovascular effects, which include increased systemic, pulmonary and left atrial BP, CVP and heart rate, and an increased susceptibility to cardiac arrhythmias. The combination of the sympathetic response and increased muscle activity from the convulsions occurring in SE results in a hyperthermic state, with the potential for body temperature to rise to life-threatening levels. The sympathetic tone also causes increased bronchial secretions and salivation that, in combination with decreased ventilation, results in respiratory compromise. An increase in CBF is also seen in the early phase of SE, probably in response to the increased metabolic demand of the neurons. Lactic acidosis occurs due to increased anaerobic metabolism resulting from the excessive muscle and neuronal activity.

As the seizure activity continues, the body's compensatory measures fail and can no longer adequately meet the increased metabolic demands of the brain. The impaired respiratory function that occurs in the early phase results in hypoxia, which is responsible for most of the continued complications. Impaired cardiac ventricular function, cardiac output and hypotension occur. As cerebral autoregulation fails, CBF becomes dependent on systemic BP, thus the systemic hypotension results in inadequate cerebral perfusion. The end result is neuronal ischaemia and cell death. The cumulative systemic hypoxia can result in multi-organ failure (**336**).



▼336 Schematic overview of the systemic effects of prolonged seizure activity.

CLINICAL PRESENTATION

Most patients experiencing SE display obvious generalized seizure activity and marked alteration in consciousness. The mean age of dogs at presentation has been estimated to be between 4.2 and 5 years (range 0.15–15 years). No statistical gender prevalence has been documented, although one study indicated a male predominance. One study found the English Foxhound, Pug, Teacup Poodle, Boston Terrier and Lakeland Terrier breeds to be overrepresented when considering SE due to multiple causes. Another study investigating seizures due to multiple causes found German Shepherd Dogs had an increased risk of experiencing SE.

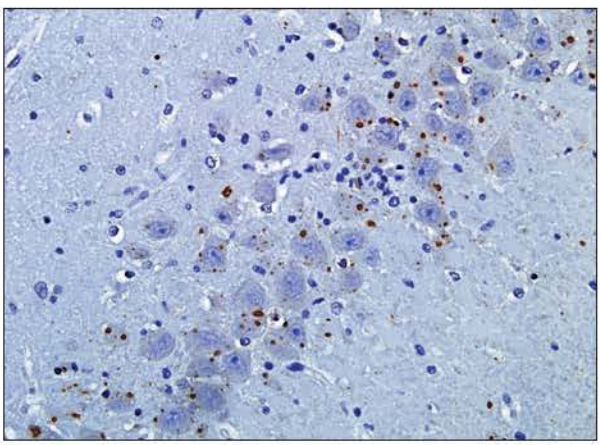
Non-convulsive SE has not been well documented in veterinary medicine, but is recognized in human medicine. In human medicine these patients are classified as having complex partial SE or absence SE and require electroencephalography for diagnosis. Focal motor seizure activity has been documented in veterinary patients and this activity may be prolonged enough to be classified as focal motor SE. Focal motor seizures may also become generalized and progress to generalized SE.

Human patients who have electroencephalographic evidence of SE with little or no visible motor activity are still at risk for CNS injury and require immediate attention. Ongoing SE can produce neuronal death in experimental models of status, even when metabolic factors are corrected, and in animals that are ventilated and paralysed. Such damage has been seen in canine experimental models of focal status as well, indicating a need for treatment of this situation.

DIFFERENTIAL DIAGNOSIS

The precipitating factors in a case of SE must always be vigorously sought and treated to facilitate seizure control and to be certain that the underlying cause is treated before it results in irreversible cerebral damage. Common disease processes associated with SE include tumours, CNS inflammatory disease (**337**), trauma, metabolic disorders such as electrolyte disturbances, and toxicities. Therefore, the presentation of a patient in SE does not imply a specific underlying disease process. Of all dogs experiencing generalized seizure activity due to any cause, up to 30% may manifest SE. A recent study documented the frequency of SE as ≤5% in dogs with idiopathic epilepsy. However, idiopathic epilepsy has been identified as the cause of SE in 27–37% of patients, some of which was associated with inappropriately low therapeutic concentrations of antiepileptic drugs (AEDs). Secondary epilepsy (e.g. brain tumours, inflammatory disease) has been identified in 32–40% of patients presenting in SE, while reactive epilepsy (systemic metabolic abnormalities and toxicities) has been documented in 7–23% of these patients. For dogs with SE with no prior seizure history, toxicity should be the primary differential.

The differential diagnoses for primary, secondary and reactive epilepsy are reviewed in more detail in Chapter 7.



▶ **337** **Hippocampus of a cat. Distinct labelling for rabies virus antigen within the perikaryon of several neurons. (*Note:* This can be a cause of status in dogs and cats in endemic regions.) (Photo courtesy Raquel Rech)**

DIAGNOSIS AND MANAGEMENT

The diagnosis, systemic management and seizure treatment detailed in the sections below should, as much as possible, be taking place simultaneously. This necessitates a 'team' or multi-person approach to the emergency seizure patient.

Diagnosis

The diagnostic protocol for a patient presenting in SE includes a thorough history to determine if toxin exposure or trauma is a possibility. On initial presentation of the patient, it is prudent to examine the skull and spine for any evidence of recent trauma (**338**). This should be done by gentle palpation of the animal, paying particular attention to the head and spine, assessing for crepitus, pain and asymmetry.

Immediate assessment of glucose, sodium and calcium levels, renal and hepatic dysfunction and serum cholinesterase levels should be performed in all SE patients. (*Note:* Liver and muscle enzymes may be increased shortly after seizure activity because of the effects of hypoxia, hypotension and convulsive activity in the case of muscle enzyme elevations.) At some point a more complete minimum database (haematology, serum chemistry, urine analysis) will help to further evaluate the patient for metabolic disturbances as an underlying cause for SE (*Table 88*) and/or evaluate for systemic damage produced by the SE event. Myoglobinuria can be seen associated with SE as a consequence of the muscle damage mentioned above. If the patient has a chronic seizure disorder and is on maintenance AEDs, blood levels of these medications should be assessed as soon as possible.

If the patient is stable enough to be anaesthetized once seizure activity has been controlled, advanced imaging with CT or MRI is recommended to determine if there is an underlying structural disease responsible for the SE. Analysis of CSF should be performed to evaluate the patient for encephalitis and consideration should be given to serum and CSF infectious disease titres and PCR analysis.

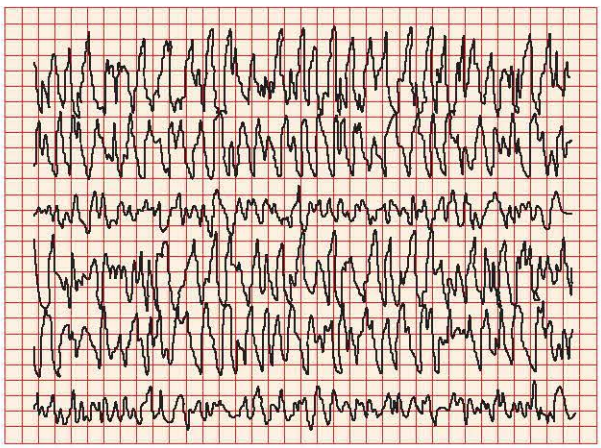
Abnormalities in imaging and CSF can be the result of SE itself. MRI lesions have been described in the piriform/temporal lobes. These lesions appear as variable hyperintense lesions on T2-weighted sequences and hypointense on T1-weighted sequences (see **131**).



▲ **338** **Lateral cervical spine radiograph of a dog that presented in status epilepticus after trauma. An atlanto-axial subluxation was discovered, presumed to be related to the initial trauma, but co-existent with the status.**

Table 88 Diagnostic investigation of status epilepticus patient

- **Arterial blood gas.** Marked metabolic acidosis is common and will resolve when patient is stabilized; respiratory acidosis needs immediate treatment.
- **Electrolyte analysis.** Treat immediately with fluid therapy.
- **Glucose analysis.** If hypoglycaemic, treat with 50% dextrose diluted to 25% (500 mg/kg IV) over 15 minutes or treat with oral glucose syrup.
- **Haematology/serum chemistry.** Can be affected by seizure activity so may need to repeat 48 hours after stabilization.
- **Urinalysis.** Rule out myoglobinuria and monitor urine output with indwelling urinary system.
- **Serum AED level.** If patient has been on AED treatment.
- **ECG.** Arrhythmias can occur up to 72 hours after the seizures due to myocardial damage.
- **Dynamic bile acid assessment.**
- **Toxicity screen.** Immediate results will not be available, but blood can be taken to submit for cholinesterase levels.
- **CSF tap.** Rule out inflammatory disease.
- **MRI/CT scan of the brain.** Rule out structural brain diseases.
- **EEG.** Documents continued seizure activity after the physical manifestations have ceased (**339**).



▲ 339 **Reproduction of an EEG from an anaesthetized dog that had been hit by a car 2 days earlier. The dog was having seizure activity prior to anaesthesia. The trace reveals diffusely abnormal electrical activity. Calibrations 20μV:1 second.**

These lesions completely or at least partially resolve with time (10 days to 18 weeks) in the absence of additional seizure activity. The signal intensities on MRI represent an increase in relative water content, suspected to be the result of vasogenic and/or cytotoxic oedema. Recently, the use of diffusion-weighted MRI has suggested that this may be a useful method for imaging SE dogs in terms of detecting underlying seizure-related pathology.

The role of the electroencephalogram

Although the initial diagnosis of SE is usually based on clinical criteria, electroencephalography has an important role in the diagnosis and management of SE. Elimination of seizure activity on the EEG is the goal in the management of SE, as seizure activity in the brain can continue even when its physical manifestations have ceased. Initially, discrete changes are seen, which may merge to form a waxing and waning pattern of rhythmic ictal discharges that ultimately continues. This continuous seizure activity, which may take the form of continuous spike or spike-and-wave patterns, rhythmic sharp waves or rhythmic slow waves, is then punctuated by periods of relative flattening that become progressively longer as the ictal discharges shorten. These patterns can be recognized in a comatose patient suggesting SE, even in the presence of extremely subtle convulsive movements (**339**). Unfortunately, a large series evaluation of EEG recordings in veterinary patients experiencing SE has not been done. However, EEG recordings should be utilized in those patients that are in a coma on presentation or after drug administration to evaluate the presence of continuing SE. If clinical seizure activity stops and the patient is clearly recovering consciousness, EEG monitoring is not necessary. Despite the many uses of the EEG, therapy for SE should not be delayed by waiting for electroencephalography results. After seizures have terminated in dogs or cats with SE, an assessment can be performed to identify the aetiological precipitating factors (see Chapter 7).

Management

An underlying disease must be identified if possible to ensure adequate therapy and, ultimately, seizure control. Treatment of the patient in SE should be focused on:

- Systemic stabilization.
- Correcting any underlying conditions.
- Cessation of the seizure activity.

These 3 areas need to be addressed at the same time, and concurrently with diagnostic investigations.

Systemic stabilization (*Tables 89* and *90*)

All of the issues below are difficult to address during SE and may improve after SE has stopped, but attempts should be made to focus on these management areas, especially when multiple drug use has been necessary.

Airway, breathing and circulation

Hypoxia may be the result of, or precipitate, SE and thus must be corrected for recovery to occur. Airway management in a patient actively having a seizure may be difficult; however, ensuring airway patency is crucial in an unresponsive patient. The level of intervention will depend on the animal's status. The airway may need to be suctioned due to production of excessive amounts of saliva. Administration of 100% oxygen via either a non-rebreathing mask or flow-by is recommended. If the patient is unresponsive, not spontaneously breathing or not ventilating adequately (high end tidal CO_2 or high $PaCO_2$), intubation and/or mechanical ventilation is/are necessary.

A large-bore intravenous catheter should be placed for administration of fluids and drugs; this is obviously not possible during SE, which initially limits the treatment possibilities.

While hypertension is usually present early in SE, hypotension can occur as the event progresses and is often exacerbated by the AEDs used. Therefore, obtaining and monitoring systemic BP is important, but is completely impractical during the seizure event. Treatment of hypertension is directed at cessation of the seizure activity. Hypotension should be treated as in any shock situation, starting with a bolus of crystalloids followed by colloids if necessary (see Chapter 31). Acidosis is far more common in SE patients than alkalosis, therefore administration of balanced electrolyte solutions is appropriate.

Acid–base status

Metabolic acidosis is common in SE patients during the convulsive episode. Resolution of the metabolic acidosis usually occurs with cessation of the convulsions. Identification of hypoxia or respiratory acidosis should result in immediate attempts to improve oxygenation via oxygen supplementation (**340**).

Table 89 Monitoring the SE patient

- **Heart rate/rhythm.** Continuous monitoring with telemetry or a least audible Doppler monitoring is preferred. Target ranges: dog, 60–120 bpm; cat, 140–180 bpm.
- **Respiratory rate.** Continuous monitoring with telemetry is preferred. Target ranges: dog, 8–34 bpm; cat, 10–20 bpm.
- **Urine production/specific gravity.** Placement of a closed urinary collection system is preferred for hygienic reasons and to allow for appropriate quantifications of 'in and outs':
  - USG: over 1.030–1.035 is concentrated, higher may indicate inadequate fluid intake.
  - Normal urine production: 1–2 ml/kg/hour.
- **Blood pressure.** Frequent monitoring with oscillometry or Doppler would be appropriate. Continuous, direct arterial blood pressure monitoring is not necessary, but can be used if an arterial line is present. The goal is to maintain systolic BP >90 mmHg (MAP 70–80 mmHg when available).
- **Oxygenation/ventilation.** Monitoring oxygenation with pulse oximetery and end tidal CO_2 is adequate, though serial blood gases are more accurate:
  - Pulse oximetry: above 95%.
  - End tidal CO_2: 35–40 mmHg.
  - PaO_2: 75–100 mmHg (arterial; on room air).
  - $PaCO_2$: 35–45 mmHg (arterial; on room air).
- **Body temperature.** A rectal probe is tolerated by many patients due to the level of sedation. Target ranges: dog, 36.9–39.2°C (98.5–102.5°F); cat, 37.8–39.2°C (100–102.5°F).
- **Neurological examination.** Imperative that these examinations are performed serially and recorded to allow for review and assessment of signs of improvement/deterioration.

Table 90 Managing the recumbent patient

- **Monitor vital parameters.** See *Table 89*.
- **Keep in well-padded cage.** Bedding should be kept clean and dry at all times. Bean beds, slings or hammocks, and mattresses can all be used to achieve adequate padding. Well-padded caging helps to prevent pressure sores.
- **Turn every 4 hours.** Helps to prevent pressure sores and atelectasis of lungs on dependent side. If possible, keep chest sternal as much as possible and continue to turn hips.
- **Lubricate eyes.** Ideally use artificial tears every 2–4 hours. Petroleum ophthalmic ointment is less good (due to build up), but possible if availability of artificial tears is limited. Prevents damage to cornea (ulceration).
- **Urination.** Place indwelling urinary collection system using sterile technique. The collection bag should be emptied aseptically every 4–6 hours as needed. Quantification of the urine allows calculation of patient 'ins and outs' and thus monitoring of renal function and hydration status.
- **Feeding/watering.** If patients are able to voluntarily eat/drink, they should be in sternal recumbency when offered food and water and ideally kept in a sternal position for 5 minutes after eating/drinking. This is to prevent aspiration of oral contents. If unable to eat and drink fluid, therapy and/or nutritional support should be addressed.
- **Thermoregulation.** Additional heat support or cooling should be provided, depending on body temperature.
- **Pressure sores.** Monitor integument 2–3 times daily. Pressure sores most often occur along bony protuberances. Areas of heat, pain, erythema, hair loss or softening of the skin are suspicious and should be clipped, cleaned and monitored. If a pressure sore develops, it should be kept clean and dry. The site should be padded (doughnut bandages are ideal, though in some anatomical locations can be difficult) to prevent worsening.



▲ 340 A dorsal pedal arterial catheter is placed to help with repeat blood gas evaluations.

Temperature regulation

Hyperthermia occurs commonly in SE patients and can be life threatening. If the temperature exceeds 40°C (104°F), passive cooling measures should be started. Continuous rectal temperature monitoring should be pursued, particularly if cooling measures are performed to prevent rebound hypothermia. Passive cooling should be stopped when the patient's temperature reaches 39°C (102°F) in order to prevent rebound hypothermia.

Identify and treat underlying conditions

A minimum database should be collected to include evaluations of glucose, electrolytes, renal and hepatic function and, if indicated, AED serum concentration.

Hypoglycaemia

If hypoglycaemia is confirmed, administration of 50% dextrose (500 mg/kg [1 ml/kg] IV) is indicated. This bolus should ideally be diluted to 25% dextrose and administered over 15 minutes. Hyperglycaemia has been linked to exacerbation of the neuronal injury of SE, therefore it is preferable that hypoglycaemia is evaluated prior to administration of an intravenous bolus. This neuronal injury is the result of the hypoxic environment and, therefore, anaerobic metabolism with lactic acidosis created by SE. Administration of thiamine (vitamin B_1) may help to counteract the detrimental side-effects of hyperglycaemia. Thiamine is a coenzyme essential for the entry of glucose into the Kreb's cycle within the brain. Giving thiamine (25–50 mg per animal IM) before the administration of a dextrose bolus is recommended. If intravenous therapy is difficult to perform, oral administration of a sugar-based syrup can be a useful substitute. Administration of oral medications should be done with caution and only attempted in a patient with an adequate degree of consciousness.

Hypocalcaemia

If hypocalcaemia is confirmed in a patient in SE, immediate therapy is indicated. Administration of 10% calcium gluconate (0.5–1.5 ml/kg IV slowly over 10 minutes) should occur. During administration, the heart rate and rhythm should be monitored, preferably with electrocardiography. The infusion should be stopped if there is any evidence of bradycardia.

Longer-term maintenance of hypocalcaemia requires oral calcium (25 mg/kg q8–12h) and vitamin D (calcitriol, 2.5–10 ng/kg q24h; dihydrotachysterol, 0.02–0.03 mg/kg q24h for 3 days then 0.01–0.02 mg/kg q6–24h) supplementation. Serum concentration of calcium should be monitored closely (every 1–3 days) and adjustments made based on the calcium concentration.

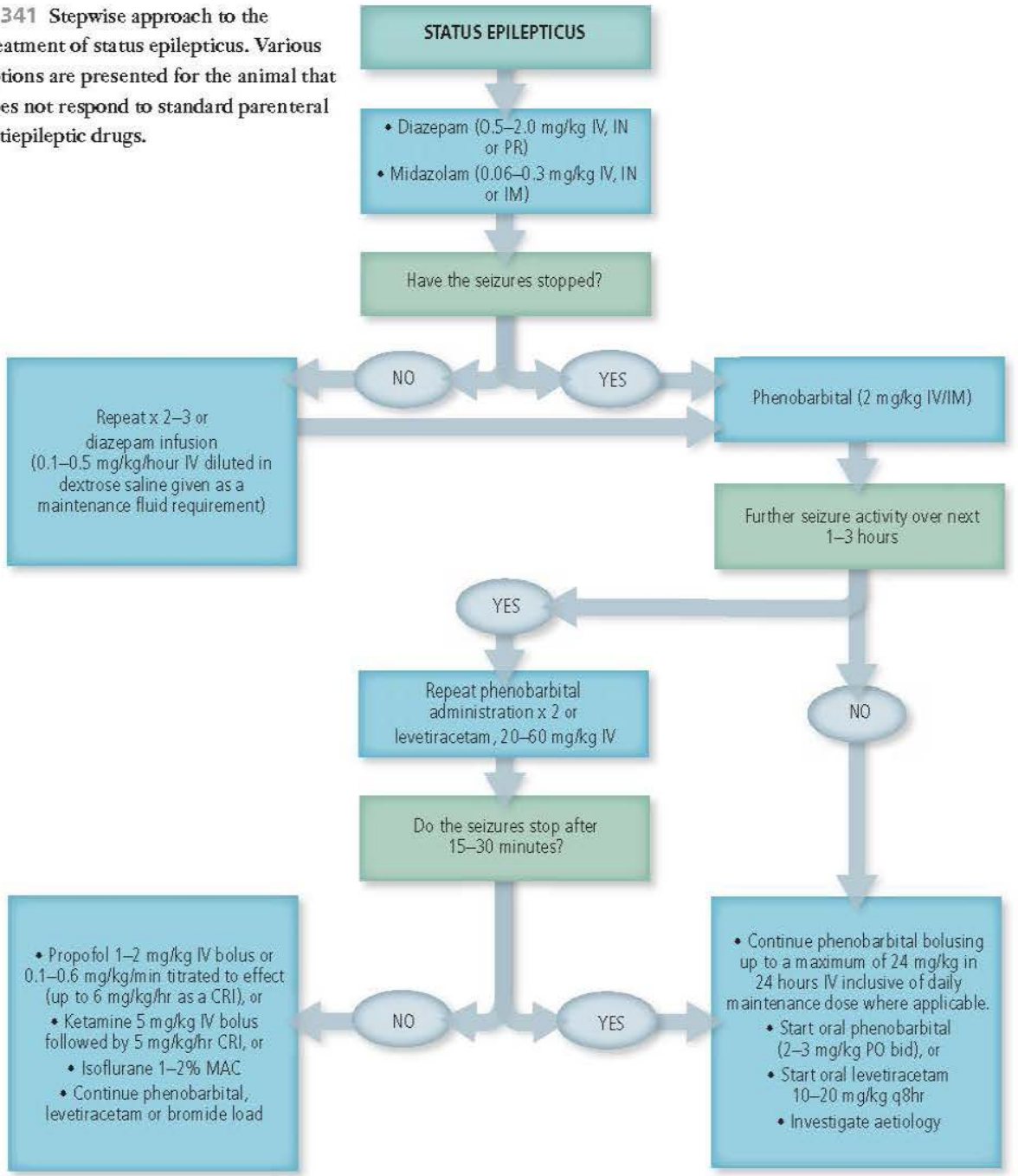
Sodium abnormalities

Abnormalities in sodium levels should be corrected slowly if there is suspicion that they have been chronically present, as rapid correction may lead to further neurological deterioration. (See Chapter 27 for further details on sodium abnormalities and their treatment.)

Hepatic encephalopathy

Hepatic encephalopathy (HE) results when the metabolic and detoxification functions of the liver are severely impaired and/or bypassed from reduced hepatic function, urea cycle enzyme deficiency or abnormal shunting of portal blood around the liver. Some of the substances implicated include ammonia, amino acids (especially the aromatic amino acids), short-chain fatty acids, mercaptans and biogenic amines. Short-term therapy of HE may include lactulose, enemas and antibiotics. (See Chapter 27 for more information.)

▶ **341** **Stepwise approach to the treatment of status epilepticus. Various options are presented for the animal that does not respond to standard parenteral antiepileptic drugs.**



Cessation of the seizure activity (341)

Administration of intravenous antiepileptic medications should be commenced immediately on attaining intravenous access in an SE patient. As intravenous access is frequently not initially possible, other routes of administration should be considered. Immediate therapy is indicated based on acceptance that the duration of SE is linked to neurological morbidity and that SE may become progressively less responsive to treatment with diazepam.

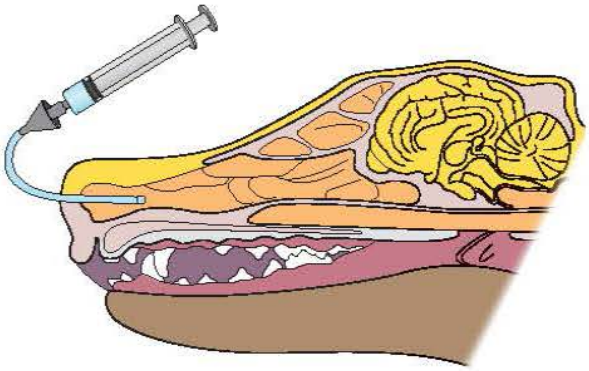
Step 1: Benzodiazepines

This class of drug includes diazepam, midazolam, lorazepam and clonazepam. They are injectable, potent and fast-acting, making them the preferred initial therapy in SE. With their effects only being temporary, a more long-acting anticonvulsant will be necessary following their use. Respiratory depression, hypotension and reduced consciousness are all possible side-effects.

Antiepileptic effects are thought to be the result of benzodiazepine-receptor-mediated enhancement of both pre- and post synaptic GABAergic transmissions. This enhanced GABAergic transmission results in increased movement of chloride ions into neurons and thus hyperpolarization of the neuron with decreased ability to form an action potential. They also limit sustained repetitive neuronal firing at higher concentrations by decreasing the spread of nerve impulses to other neurons. It is thought that benzodiazepines prevent the spread of seizure activity rather than suppress the epileptic focus.

Diazepam (0.5–2.0 mg/kg IV up to 20 mg maximum dose)

Diazepam is metabolized in the liver by hepatic microsomal systems. The major metabolites (nordiazepam, oxazepam) have 33% of the activity of their parent drug. Diazepam has a short elimination half-life in the canine patient (3.2 hours), although the half-lives of the metabolites are slightly longer (oxazepam, 5.2 hours). Because of its short elimination half-life it is not an appropriate choice for chronic management of seizure patients. Mean peak plasma concentrations are reached in less than 2 minutes when diazepam is administered intravenously.



▲ 342 **Intranasal administration of benzodiazepines can result in rapid cerebral concentrations of the drug due to the highly vascular nature of the turbinates. This avoids the first-pass metabolism associated with intravenous administration.**

Intravenous administration of diazepam is preferred; however, if intravenous access is not available, it may be administered rectally or intranasally (**342**). Intramuscular absorption of diazepam is variable, therefore this route of administration is not recommended. Rectal administration results in adequate absorption, with peak plasma concentrations reached within 15 minutes. (*Note:* Patients on long-term phenobarbital therapy may require higher doses of diazepam [2 mg/kg] due to activation of the liver's hepatic cytochrome P-450 enzyme system resulting in increased metabolism of diazepam and its metabolites.) Target plasma concentrations are reached in approximately 10 minutes in animals that are not being treated with phenobarbital and by 20 minutes in animals on chronic phenobarbital therapy.

If 1–2 doses of diazepam fail to control the seizure manifestation, the addition of another, longer-acting anticonvulsant medication should be immediately considered; however, it should be remembered that these drugs can take a short time to become effective. Continued administration of diazepam, in the face of failure to control seizure manifestation, may result in further neurological compromise to the patient from the seizure activity as well as toxicity from diazepam. Administration of diazepam in cats has been associated with acute hepatic necrosis; however, this complication has only been reported when diazepam was administered orally, therefore parenteral administration of diazepam in the emergency situation should not be withheld from feline patients.

If a bolus of diazepam does work, a CRI should be considered (0.1–0.5 mg/kg/hour) in the interim prior to the longer-acting anticonvulsant becoming effective. A syringe pump can be used or the diazepam can be diluted in 5% dextrose in water (D5W) such that the total volume administered is equal to the patient's maintenance fluid requirement over the hour. Concerns regarding aqueous solubility, formation of deposits and adsorption onto polyvinyl chloride tubing have been raised. Compatibility should be checked before combining diazepam with any other medication or intravenous fluid, as formation of precipitates is common. Drugs should never be administered if a precipitate forms. The use of midazolam in lieu of diazepam circumvents many of these concerns, but this drug can be more expensive. If diazepam is used, the administration set should be protected from light and changed every 2 hours. Care should also be taken when administering other medications into this line, as many medications will cause precipitates to form when combined with diazepam.

A high initial rate is used following a bolus dose and is usually continued for up to 6 hours before a gradual and tapered (50% every 6 hours) reduction is begun. This approach is useful if SE is due to toxicity, where seizures will probably be present for a protracted time period, or while awaiting a loading dose of phenobarbital to become effective.

Midazolam (0.06–0.3 mg/kg IM or IV)

Midazolam's peak plasma concentration in dogs after intramuscular injection is 15 minutes and its half-life in dogs is 1–2 hours. Midazolam's superior absorption and bioavailability with intramuscular injection when compared with diazepam make it a feasible alternative when there is no intravenous access on initial presentation.

Step 2: Barbiturates

Following the successful use of benzodiazepines, barbiturates should be considered as long-term maintenance anticonvulsants. They can be parenterally loaded to achieve a rapid steady state serum concentration. Loading phenobarbital is usually only performed in those patients that have not previously received this drug or are suspected to have low serum drug levels. If bolus doses of benzodiazepines did not stop the seizure activity or were only temporarily successful, barbiturates become the next therapeutic option. Phenobarbital is the most commonly used barbiturate for acute seizure control. Barbiturates are metabolized in the liver, predominantly through hydroxylation. The post-synaptic enhancement of the inhibitory effects of GABA is the primary mechanism of action. This effect results in an increased seizure threshold as well as a reduction in spread of the seizure.

The loading dose of phenobarbital is 12–24 mg/kg IV. However, it is recommended that smaller boluses (2–4 mg/kg) should be administered, repeating every 20–30 minutes, to effect, but not exceeding 24 mg/kg over 24 hours. The parenteral form of phenobarbital may also be used intramuscularly, which is useful in the initial treatment of a case that does not have intravenous access. However, the distribution of phenobarbital to the CNS and hence its effect may take up to 30 minutes due to its low lipophilicity. Intramuscular administration may avoid the profound respiratory and cardiovascular depression experienced when phenobarbital is administered following benzodiazepines.

Side-effects of phenobarbital include respiratory depression, hypotension and sedation. In an SE patient, whose respiratory and cardiovascular function may already be compromised, these side-effects could become life threatening, thus monitoring of respiratory and cardiovascular parameters must be continuously performed.

Parenteral use of this drug should be followed as soon as possible by the more routine twice daily oral administration, to ensure long-term control of seizure activity is addressed.

Step 3: Levetiracetam

If the use of phenobarbital is not successful or is considered inappropriate (e.g. underlying presence of liver disease), the next option is the use of levetiracetam. Levetiracetam (20–60 mg/kg IV) is a newer anticonvulsant and has a half-life of 3–4 hours in dogs. Its intravenous use may be effective for 8 hours, at which time it can be repeated. While the binding site of the drug, a site on a synaptic vesicle protein in neurons, has been identified, the exact mechanism of action is unknown. It is thought to act by modifying calcium-dependent exocytosis of neurotransmitters and may therefore be synergistic with phenobarbital or potentially effective where phenobarbital has not been. When used with phenobarbital, a dose of levetiracetam at the upper end of the range may be necessary. Levetiracetam causes minimal

sedation, making it desirable in treating more refractory SE patients that already have an altered consciousness. It is not metabolized in the liver and so represents a more suitable option than phenobarbital for dogs and cats with portosystemic shunts or liver disease. Excretion is purely renal and therefore there are minimal interactions with other anticonvulsant medications; however, caution should be used in patients with deficient renal function. Levetiracetam may also have neuroprotective effects, reducing seizure-related brain damage. As with phenobarbital, the oral maintenance use of levetiracetam should follow its parenteral use once SE has been controlled.

Step 4: Short-acting anaesthetic agents

SE that does not respond to a benzodiazepine, phenobarbital or levetiracetam is considered refractory and requires more aggressive treatment. Potential reasons for resistant seizure activity include inadequate anticonvulsant doses, an uncorrected metabolic abnormality or the presence of an intracranial disease, such as a tumour. These patients often represent a difficult therapeutic problem. Short-acting anaesthetic drugs are the most commonly used agents for treating resistant SE, as they have a rapid onset of action and short half-lives and cause reductions in cerebral metabolic rates. These drugs should be used only in an intensive care setting because of the need for continuous BP monitoring and, ideally, CVP monitoring.

Propofol (1–2 mg/kg IV bolus or 0.1–0.6 mg/kg/minute titrated to effect, up to 6 mg/kg/hour as a CRI)

Propofol acts on the GABA receptor in a similar way to both barbiturates and benzodiazepines and so has anticonvulsant actions as well as being an anaesthetic. It also reduces the metabolic demand of the CNS. Its metabolism is predominantly through hepatic mechanisms and is far more rapid than that of barbiturates. This drug can be successfully used in SE cases due to toxin exposure and while awaiting more effective steady state levels of phenobarbital or bromide (see below).

The primary side-effect of propofol is apnoea, which may result in hypoxaemia if not treated appropriately. Thus, if a CRI of propofol is used, adequate airway control, haemodynamic support and possible ventilatory support should be available.

In human medicine, a propofol infusion syndrome has been reported when propofol has been used at high doses (>4 mg/kg/hour) or for prolonged periods (>48 hours). Signs of this syndrome include metabolic acidosis, rhabdomyolysis, hyperkalaemia, lipaemia, renal failure, hepatomegaly and cardiovascular collapse. While this syndrome has not been reported in veterinary patients, the possibility exists, especially in those patients maintained on a CRI long term. (*Note:* Propofol is a phenol and therefore capable of causing oxidative injury to RBCs of the cat, resulting in Heinz body formation and haemolytic anaemia.)

Ketamine (5 mg/kg IV bolus followed by 5 mg/kg/hour CRI)

Ketamine is an NMDA receptor antagonist. NMDA receptor antagonists, like ketamine, are able to end the maintenance phase of chronic SE, sometimes called self-sustaining SE. NMDA receptor activation only occurs in the later phases of SE, perpetuating the seizure activity, so NMDA antagonists are suspected to be beneficial during prolonged or refractory SE. Ketamine may also have neuroprotective effects by inhibiting NMDA receptor-mediated excitotoxicity associated with prolonged seizure activity; however, there is also some evidence that excessive antagonism of the NMDA receptors can be detrimental. Although the use of ketamine has been documented in a dog with SE, there are currently no clinical studies documenting the effectiveness or safety of ketamine CRI in treating veterinary patients.

Step 5: Inhalant anaesthesia

Inhalant anaesthesia is considered a last resort in refractory SE. Not all volatile anaesthetics are appropriate in managing the SE patient. For example, enflurane may increase seizure activity. Isoflurane and sevoflurane may attenuate seizure activity, as has been shown in cats with experimentally induced seizures. The utility of this approach is in the cessation of the physical manifestations of SE while a maintenance anticonvulsant takes effect. Maintaining a patient on an inhalant anaesthetic requires intensive monitoring and mechanical ventilation. During this time, phenobarbital, levetiracetam or bromide should be given at a loading dose to achieve a steady state, at which time the inhalant anaesthetic can be withdrawn to assess seizure control.

Step 6: Recovery/maintenance

Dexmedetomidine

Some patients will display marked agitation on recovery. The use of dexmedetomidine as a CRI (0.1–1.0 µg/kg/hour) has been reported to help manage this issue. However, caution must be used as dexmedetomidine may cause bradycardia, arrhythmia (AV block), decreased respiration and hypothermia, which can be problematic in the SE patient, therefore the dose should be adjusted following careful monitoring.

Vital parameters, including heart rate, BP, ventilation and body temperature, should continue to be monitored and serial neurological examinations performed until the patient is mentally alert and mobile. The combination of SE and the previously mentioned medications can result in marked cardiovascular and respiratory depression as well as hypothermia. It is imperative that the clinician monitor parameters to ensure systemic support is continued as needed for a complete recovery.

Once seizure activity has been controlled and systemic stabilization has been ensured, a maintenance AED will need to be considered. In a naïve patient, phenobarbital may be used as the sole medication. It is recommended that a patient with a history of SE be loaded so that steady state serum levels are reached as quickly as possible. Instructions for loading phenobarbital have been given above. If the animal was on phenobarbital prior to the episode of SE, two options exist:

- If the animal's serum phenobarbital level is low, an increase in dose may be indicated.
- If the serum level is well within the therapeutic range, is approaching toxic levels or if the patient is displaying adverse effects, an additional AED may be added. Add-on AED drugs include bromide (20–30 mg/kg q24h, and can be loaded at 600 mg/kg over 4 hours to 4 days; rapid administration can result in coma), zonisamide (8–12 mg/kg PO q8h), levetiracetam (7–20 mg/kg q8h), gabapentin (10–30 mg/kg q8h) and pregabalin (2–4 mg/kg q8–12h).

(See Chapter 7 for additional information on maintenance seizure medications.)

Bromide

Potassium bromide (KBr) is a recommended maintenance AED in the dog. It is not used in the cat because of the risk of inducing allergic pneumonitis. The half-life of KBr after its oral administration in the dog is approximately 25 days, which has precluded its use in SE. Recent work has established that KBr is well absorbed after rectal administration, with an estimated bioavailability of 57.7% and a mean half-life of 20.4 days. For a more rapid effect than that obtained with oral maintenance dosing regimens, a rectal loading protocol has been devised. Intrarectal administration may be preferred in the patient that is heavily sedated from prior diazepam and phenobarbital administration. A loading dose of KBr (600 mg/kg) can be administered over a 24 hour period as 6 per rectal boluses (100 mg/kg q4h). The side-effects seen with the use of this regimen may be transient diarrhoea and sedation. The use of sodium bromide may be considered, as it can be administered intravenously at a loading dose of 900 mg/kg over 24 hours and then continued at 30 mg/kg/day orally.

Zonisamide

The exact mechanism of action of zonisamide is unknown. It is thought to produce its antiepileptic effect by blocking sodium channels and reducing transient ion currents, thus stabilizing the membranes and suppressing potential hypersynchronization. The half-life is 15 hours, therefore it can be used twice daily, reaching steady state within 3–5 days. It is a sulphonamide drug and should not be administered to a dog with a history of reactions to this class of drug. It is also a known teratogen and so should be avoided in breeding animals. Most of the drug is excreted through the kidneys, with some hepatic metabolism. Minimal sedation is seen with this medication. Doses have been reported as 10 mg/kg PO q12h and 8–12 mg/kg PO q12h. It should be made clear to owners that the use of this medication in veterinary medicine has been limited and therefore its effectiveness and potential side-effects are not fully understood.

Levetiracetam

Levetiracetam's supposed mechanism of action has been discussed above. As a maintenance AED, administration three times daily is required, potentially making this drug less desirable to owners. A dose of 20 mg/kg PO q8h has been reported. Like zonisamide, there is limited experience of using this medication in veterinary medicine. Sedation is minimal.

Gabapentin

The mechanism of action resulting in gabapentin's antiepileptic effects is not fully understood. While gabapentin is structurally related to the neurotransmitter GABA, it does not appear to exert its effects through the same mechanism. It does not alter GABA binding, reuptake or degradation, nor does it serve as a GABA agonist within the body. The half-life in dogs is about 2–4 hours, making three times daily administration necessary, but steady state serum levels are reached quickly (10–20 hours). Gabapentin is eliminated by the kidneys unchanged. Administration of 10–20 mg/kg q8h for both dogs and cats has been recommended. Side-effects are uncommon, with sedation the most likely.

Pregabalin

The mechanism of action of pregabalin is unknown, but its chemical structure is related to that of gabapentin. It may modulate calcium influx into neurons, reducing excessive neurotransmitter release. The recommended oral dose is 2–4 mg/kg q8–12 h (twice daily is thought to be sufficient for most dogs). Sedation is the most commonly reported side-effect. Like zonisamide, levetiracetam and gabapentin, pregabalin has had limited use in veterinary medicine.

PROGNOSIS

One study reported a 25% mortality rate for dogs presenting with SE or cluster seizures, while another study documented a 5% mortality rate and a 33% euthanasia rate in dogs with SE of multiple causes while in hospital. However, an unbiased mortality rate for dogs is unknown given that many patients are euthanized prior to aggressive treatment and diagnostic testing, and SE is due to multiple types of brain disease (**343**). Dogs with SE of all causes that die or are euthanized after discharge have a survival time of 0.1–5.9 years (median 0.8 years).

Factors reported as negatively affecting outcome are the diagnosis of symptomatic epilepsy (e.g. due to GME or cerebral neoplasia) and failure to adequately control the seizure activity within 6 hours of its onset. Dogs with SE due to toxicosis have more favourable outcomes than dogs with symptomatic epilepsy. No associations have been made correlating breed and age with type of seizure activity observed.

The mean hospitalization time for dogs with SE has been reported as 51.6 ± 42.6 hours. Recurrent SE is a possibility even after initial stabilization and hospitalization. Both these factors have important financial implications that the owner should be made aware of.



▶ **343** Morbidity following prolonged status epilepticus, such as the aspiration pneumonia evident on this lateral radiograph, can be a reason for euthanasia.

THE OUT-OF-HOSPITAL STATUS EPILEPTICUS PATIENT

In out-of-hospital situations there are often inadequate resources to manage the potential complications of intravenous therapy. In these situations, severe systemic and cerebral damage may result, which can lead to death in some dogs. However, if prompt pre-hospital seizure treatment can be given, fewer AEDs are required and seizures tend to be shorter. Rectal, intranasal and buccal/sublingual routes of administration may be useful in these settings, especially as the absorbed drug bypasses the liver, thus avoiding the problem of first-pass metabolism. As both intravenous and intramuscular injections during SE can pose risks to the patient and the caregiver and are often difficult to achieve, per rectal and intranasal routes of administration need to be considered.

The use of benzodiazepines by the routes discussed below is not licensed, therefore they need to be used with caution. The at-home treatment of seizures is not meant to avoid immediate veterinary attention for systemic stabilization, and this must be made clear to the owner. Indications for immediate veterinary attention should be discussed with the owner and these may include: seizures that do not respond to the at-home therapy prescribed within 10 minutes; seizures that respond but recur within 24 hours; and systemic concerns such as depressed respiratory effort, obtundation and blindness. The dangers of being in close contact with a seizuring dog should also be emphasized to the owner.

Rectal administration

Rectal administration of an AED is useful in emergency situations, and it is relatively easy to carry out in the home environment. It has been well established that absorption of lipid-soluble drugs by the membranes of the colon and rectum is rapid and complete. Diazepam can be administered into the rectum using plastic administrators such as tom-cat catheters with a water-soluble lubricant. The efficacy of rectally delivered diazepam in SE depends on several factors: the time that it takes for the drug to reach the therapeutic concentration and exactly what the therapeutic concentration is in an individual dog. The actual therapeutic level in dogs has not been well documented and may be anywhere from 300 to 1500 ng/ml.

The use of diazepam administered rectally at home for cluster seizures in dogs has been evaluated and it resulted in fewer seizures per cluster, reduced owner cost for emergency room visits and good owner compliance.

The effect of concurrent long-term oral phenobarbital administration on rectally delivered diazepam has recently been evaluated. The mean peak concentration of benzodiazepine after rectal administration of diazepam in six dogs fell from 629 ng/ml to 274 ng/ml when the dogs were given phenobarbital (2.5 mg/kg every 12 hours for 30 days). These results demonstrate that dogs receiving chronic phenobarbital therapy may require a higher dose (1–2 mg/kg) of rectally delivered diazepam than those dogs that have not been previously treated with this drug. This phenomenon is due to the increased activity of the hepatic microsomal enzyme system caused by phenobarbital administration.

Rectal administration of midazolam in humans has been shown to be safe and effective, with peak plasma concentrations occurring within 10 minutes after administration.

Intranasal administration

In recent years, intranasal drug administration for systemic effects has received increased attention because of its convenience and reliability. Intranasal anticonvulsants have been used successfully in human SE cases. Midazolam has been shown to be quickly absorbed by the nasal mucosa and to reach levels that equal or substantially exceed threshold levels for sedation in humans. The duration of action following intranasal administration is similar to that after oral dosing, although the onset of action is earlier. Peak plasma concentrations occur 10 minutes after administration in dogs; plasma concentrations of midazolam exceeding therapeutic values were seen within 3 minutes after intranasal administration to children.

It has also been suggested that drugs instilled into the nasal cavity may directly reach the brain via the cribriform plate and that the concentration in the CNS may be higher than that reflected by measurements of plasma concentrations. Further studies to better understand uptake and absorption from the nasal cavity are required.

MYASTHENIA GRAVIS

Kerry Smith Bailey

INTRODUCTION

Myasthenia gravis (MG) is literally defined as 'serious muscle weakness' and is associated with failure of NM transmission. There are two types of MG: congenital and acquired.

Congenital MG (CMG) is a rare disease and is defined as an inherited disorder in which the safety margin of NM transmission is compromised by one or more specific mechanisms; it can arise from presynaptic, synaptic or postsynaptic defects. Clinically, patients with CMG present similarly to patients with acquired MG (AMG), with the chief complaints being exercise intolerance and weakness.

In its acquired form, MG is an immune-mediated disorder in which antibodies are targeted against the nicotinic acetylcholine receptor (AChR) of skeletal muscle. This results in muscular weakness and excessive fatigability. AMG is the most common NM disorder diagnosed in the canine patient, with three clinical syndromes: focal, generalized and acute fulminating:

- Focal AMG presents as localized weakness of oesophageal, pharyngeal, laryngeal and/or facial muscle groups, with no clinical evidence of appendicular weakness.
- Generalized AMG is defined by the presence of obvious appendicular weakness with or without megaoesophagus and facial, pharyngeal or laryngeal weakness.
- Acute fulminating AMG is characterized by a rapid onset and progression of profound appendicular muscular weakness, with varying degrees of facial, pharyngeal, oesophageal and laryngeal weakness. This form is often rapidly fatal due to the progression of tetraparesis and respiratory failure associated with diaphragmatic and intercostal muscle weakness.

AETIOLOGY/PATHOPHYSIOLOGY

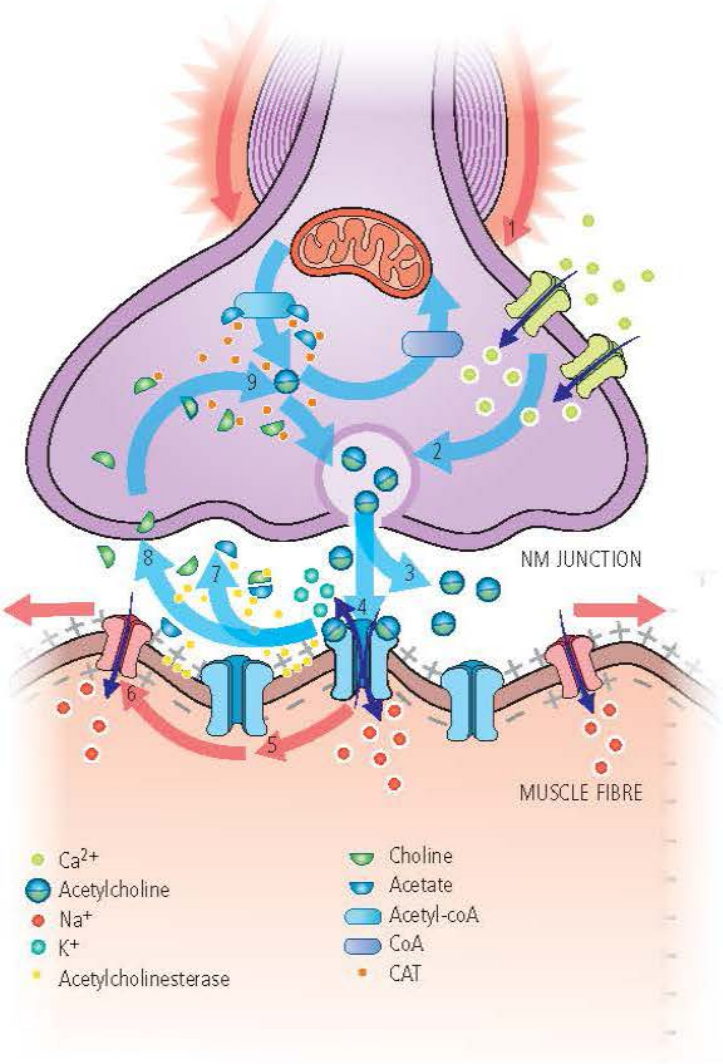
Normal neuromuscular transmission

A clear understanding of the anatomy and physiology of the normal NM junction is imperative to understand MG's pathophysiology. A motor unit consists of a motor neuron and the muscle fibres innervated by the axonal terminals of that neuron. The strength of a muscle contraction depends on the number of motor units activated within the muscle. The NM junction consists of three components: the motor nerve terminal, the synaptic cleft and the muscle end plate.

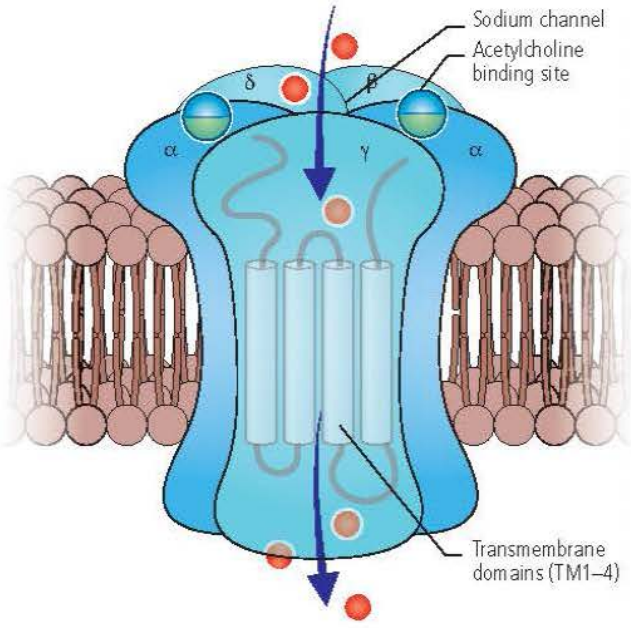
The release of ACh from the motor nerve terminal ensures a unidirectional conduction from the axon terminal to the muscle end plate. Located within the presynaptic axoplasm are vesicles, 300–500Å in diameter, that contain ACh. Each vesicle contains one quantum of ACh, or 5,000–10,000 molecules. Approximately 1,000 quanta are located adjacent to the cell membrane and are available for immediate release. Many more are contained in store and move toward the membrane to replace the liberated ACh. Each ACh quantum liberated from the nerve terminal contains a nearly equal number of ACh molecules. The nerve endings contain high concentrations of choline acetyltransferase, which synthesizes ACh, and acetylcholinesterase (AChE), which hydrolyzes ACh.

When the action potential reaches the nerve terminal, the resultant depolarization of the distal region of the axon initiates an influx of Ca^{2+} into the motor axons. The increased amount of Ca^{2+} accelerates the fusion of the vesicle membranes with the nerve terminal membrane, which leads to a large increase in the rate of ACh release. The ACh molecules traverse the synaptic cleft to reach the AChR, which is located in the end plate region of the skeletal muscle fibre (**344**, next page).

▶ **344** Sequence of events at the neuromuscular junction leading to an action potential in the muscle fibre plasma membrane. (1) Action potential increases the permeability of the motor neuron terminals to Ca^{2+}. (2) Ca^{2+} enters the terminals and triggers exocytosis of acetylcholine-containing vesicles. (3) Acetylcholine diffuses to the muscle nicotinic acetylcholine receptors. (4) Two molecules of acetylcholine bind to these receptors, increasing the Na^+ and K^+ conductance of the membrane. (5) The resultant influx of Na^+ produces a depolarizing potential – the end plate potential. (6) The current sink created by this local potential depolarizes the adjacent muscle membrane to its firing level and the voltage-gated Na^+ channels open, leading to propagation of the action potential in the muscle membrane. (7) The acetylcholine is then removed from the synaptic cleft by the enzyme acetylcholinesterase and hydrolysed to choline and acetate. (8) Choline is actively taken up via a transporter into the cholinergic axon terminal. (9) Acetylcholine is synthesized from choline and acetyl-coenzyme A (acetyl-CoA), catalysed by the enzyme choline acetyltransferase (CAT). Acetyl-coA is synthesized in the cell mitochondria when the acyl group in acetate bonds to the carrier molecule Coenzyme A (CoA).



▶ **345** Schematic diagram of the nicotinic acetylcholine-gated ion channel. The receptor channel consists of five subunits arranged around a central cation (Na^+) channel. When two molecules of acetylcholine bind to portions of the α-subunits exposed to the membrane surface, the ion channel opens and Na^+ enters the muscle cell. The subsequent depolarization of the end plate region is referred to as the end plate potential.



The AChR is a nicotinic acetylcholine receptor. It is a transmembrane glycoprotein with five subunits (α x 2, β, γ and δ) that form an ion channel (**345**). Binding of two ACh molecules to specific sites on each of the two α subunits opens the ion channel. This allows cations (specifically Na^+) to flow through the postsynaptic membrane into the muscle cell. This depolarization of the end plate region is known as the end plate potential (EPP). When the EPP exceeds the excitability threshold of the muscle cell, voltage-dependent Na^+ channels open, leading to the generation of an action potential. This propagation of the muscle potential activates the contractile elements within the muscle cell through excitation–contraction coupling.

Excitation–contraction coupling links the electrical and mechanical activity of NM transmission and represents the spread of the action potential from the motor end plate to the transverse tubules, thus initiating muscle contraction. A molecular change of the depolarized membrane results in a selective increase in Na^+ conductance, followed by an increase in K^+ conductance. Provided depolarization reaches the critical value, this molecular change (inherent in the muscle membrane) occurs regardless of the nature of the stimulus. While the action potential itself is an all-or-none phenomenon (represented as amplitude), the latency of the action potential can change depending on the speed of the initial depolarization. This variability forms the basis of 'jitter' in single-fibre electrodiagnostic studies, which will be discussed in more detail in the diagnostic section. Jitter serves as a sensitive measure of subtle changes within the end plate.

The muscle fibre membrane at the end plate is lined with a basal lamina containing the enzyme AChE. This enzyme splits the unbound ACh molecule into choline and acetate. It is located mainly in the troughs of the junctional folds of the muscle membrane. The concentration of AChE is several-fold lower than the concentration of AChRs, but it is adequate to hydrolyse most of the ACh released by the nerve terminal and to prevent repeat binding of ACh to the AChRs.

Pathophysiology of myasthenia gravis

The fundamental difference between CMG and AMG lies in the pathophysiology. CMG is the result of a single, or combination of, presynaptic, synaptic or postsynaptic defect(s). Presynaptic defects, such as mutations in the choline acetyltransferase gene, or synaptic defects due to mutation of the AChE-associated collagen gene are occasionally the cause in human CMG. More commonly, the defect is related to the amount of AChR expressed on the postsynaptic region of the NM junction. Proposed mechanisms for the AChR deficiency in canine CMG include deficient synthesis of AChR, defects in the membrane insertion of the receptor, acceleration of its degradation, decrease in its binding affinity for ACh or a structural abnormality of the NM junction. An absolute deficiency of AChR molecules in the NM junction, not just a failure of AChR to bind ACh and its ligands, has been demonstrated in the Jack Russell Terrier and Springer Spaniel.

In AMG the deficiency of AChR is due to a heterogeneous group of autoantibodies (mostly immunoglobulin class G) produced against the receptor. A specific region of the α subunit on the AChR has been found to be the binding site for most of the antibodies in AMG; this region is known as the main immunogenic region (MIR). The MIR is separate and distinct from the AChR binding sites. There is one MIR on each of the 2 α subunits in an AChR and it is located on the extracellular surface of the AChR, making it readily accessible to circulating antibodies. Mature AChRs are continuously turned over by internalization and degradation and replaced by new AChRs; they are not reused or recycled. Antibody–receptor complexes may lead to impairment of the NM transmission by encouraging endocytosis of the AChR, activating complement-mediated destruction of postsynaptic muscle cell membrane near the AChR, decreasing synthesis and membrane incorporation of new AChR, and directly interfering with AChR function by bound antibody. Regardless of the exact mechanism, the result is a decreased number of functional AChRs, which results in decreased NM transmission. The common clinical sign of exercise intolerance or fatigability is secondary to the depletion of the stores of ACh, compounded by the reduced number of functional receptors being bound with ACh molecules and also being desensitized to further stimulation.

CLINICAL PRESENTATION

Acquired myasthenia gravis

AMG has been reported in dogs ranging in age from 7 weeks to 15 years, with all breeds and both genders potentially affected. Breeds with the highest risk for AMG are Akitas, several Terrier breeds, Scottish Terriers, German Shorthaired Pointers and Chihuahuas. German Shepherd Dogs, Golden Retrievers, Labrador Retrievers and Dachshunds are most commonly documented, but this may reflect their popularity. A familial predisposition has been suggested in Newfoundlands and Great Danes. A bimodal age of onset with peaks of incidence at approximately 3 and 10 years of age has been reported in affected dogs. Rare cases of juvenile-onset autoimmune MG have also been documented.

The typical presentation of a dog with AMG is episodic, generalized muscle weakness (most obvious in the appendicular muscles) that is worsened by activity and might be relieved with rest. Some dogs present so profoundly weak that rest does not improve their condition, so this should not be a definitive criterion for diagnosis. At times, the weakness may be confined to the hindlimbs only, often mimicking an orthopaedic disorder or possibly a spinal cord disorder. Thorough neurological and orthopaedic examinations are helpful in differentiating between the three. In addition, dogs may present with regurgitation due to a megaoesophagus or dysphagia secondary to pharyngeal dysfunction. In dogs with focal MG, this might be the only clinical sign. Megaoesophagus is a relatively common finding in canine myasthenic patients (84% of all dogs with AMG present with megaoesophagus) since the majority of the canine oesophagus is skeletal muscle. Owners may note a recent voice change as a result of laryngeal muscle weakness. Urinary incontinence is occasionally seen because the external urethral sphincter also is skeletal muscle.

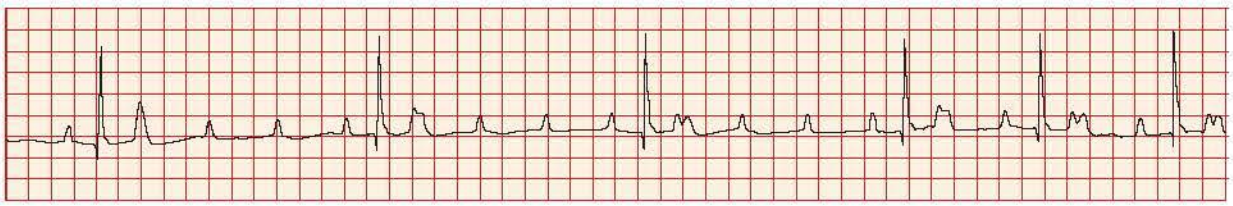
Spinal reflexes and proprioceptive testing usually remain normal, but dogs with profound weakness might appear to have poor paw positioning and/or hopping response. Cranial nerve examination is usually normal, although some dogs with AMG will exhibit a decremental palpebral reflex, indicating facial muscle fatigue.

Dogs with acute fulminating AMG can present collapsed in respiratory distress. These dogs often develop a rapid onset of oesophageal dilation, tetraparesis, pharyngeal dysfunction and loss of strength in the intercostal and diaphragmatic muscles. This can lead to aspiration pneumonia and potentially respiratory failure.

Several conditions have been associated with canine AMG, including other autoimmune disorders and neoplastic disorders. Autoimmune disorders reported to occur concurrently with AMG include hypothyroidism, hypoadrenocorticism, thrombocytopenia, haemolytic anaemia, polymyositis and inflammatory bowel disease. AMG has been linked to paraneoplastic syndromes secondary to thymoma, osteosarcoma, cholangiocellular carcinoma, anal sac adenocarcinoma and cutaneous lymphoma. Cranial mediastinal masses and thymomas have been associated with AMG in humans, dogs and cats. Thymoma cells may express antigenic epitopes similar to those of nicotinic AChRs. The immune response to these epitopes results in the lack of functional AChRs in skeletal muscle.

Third-degree heart block (**346**) has been detected in a limited number of dogs with AMG and potentially results from circulating autoantibodies directed against the cardiac conducting tissue. Since generalized weakness is a clinical sign of both AMG and third-degree heart block, both NM and cardiac diagnostic evaluations are indicated in these patients.

AMG is rare in cats. Purebred cats are overrepresented, specifically the Abyssinian and Somali breeds. Similarly to dogs, there is a bimodal distribution for the age of onset of clinical signs in cats, with peaks occurring at 2–3 and 9–10 years of age. The generalized form is the most common clinical presentation of AMG in cats. Approximately 40% of cats with AMG have a megaoesophagus, a lower prevalence than seen in dogs; this is probably due to the fact that the feline oesophagus has a smaller skeletal muscle component. The three clinical syndromes of AMG (focal, generalized and acute fulminating) have all been reported in cats. Therefore, clinical signs can include regurgitation, dysphonia, decreased palpebral reflex, decreased menace response and respiratory distress. Some cats present with cervical ventroflexion and a dropped jaw (**347**). Also unique to cats is an association between the development of AMG and treatment of hyperthyroidism with methimazole. This is known as acquired drug-induced MG. Feline AMG has been associated with the presence of a cranial mediastinal mass, though this is not associated with an increase in severity of clinical signs.





▲ 346 Electrocardiogram depicting a dog with third-degree heart block. The p waves and QRS complex bear no relationship to each other.

◀ 347 Adult cat exhibiting extreme weakness and cervical ventroflexion.

Congenital myasthenia gravis

CMG has been reported in the Jack Russell Terrier, Springer Spaniel, Smooth-haired Fox Terrier, Gammel Dansk Honsehund breeds, two unrelated mongrel dogs, and the Miniature Short-haired Dachshund as well as several cats. Multiple cases often occur within a single litter and a recessive mode of inheritance has been suggested. These dogs are young, between 6 and 12 weeks old, when they present with clinical signs consistent with NM weakness. Megaoesophagus occurs less commonly in CMG when compared with AMG, having only been reported in the Smooth-haired Fox Terrier, where an early sign of disease typically is stiffening of the hindlimbs when walking. Affected dogs frequently sit with their stifles in extension. They may progress to the point where they are unable to hold their head up, using their nose as support.

DIFFERENTIAL DIAGNOSIS

Other NM disorders may mimic MG, including botulism, polyradiculoneuritis, tick paralysis or infectious neuropathies/myopathies, and should be considered when diagnosing MG.

DIAGNOSIS

Acquired myesthenia gravis

Diagnosing AMG in dogs and cats can prove to be a difficult task. Signalment, history, clinical signs and examination findings may provide a strong index of suspicion for a diagnosis of AMG; however, additional diagnostics are required for a more definitive diagnosis.

Initial diagnostic tests

Because AMG can mimic other NM diseases, diagnosis begins with attaining a minimum database including a CBC, chemistry profile and urinalysis. Although none of these tests are definitive for AMG, other causes of generalized weakness may be ruled out (e.g. electrolyte disturbances or hypoglycaemia). In addition, the minimum database will provide baseline health screening that will be helpful in guiding diagnostics requiring general anaesthesia and designing therapeutic protocols. Occasionally, serum CK is mildly to moderately elevated in dogs with AMG, secondary to muscle cell damage as a result of falling down or being recumbent.

Presumptive diagnostic tests

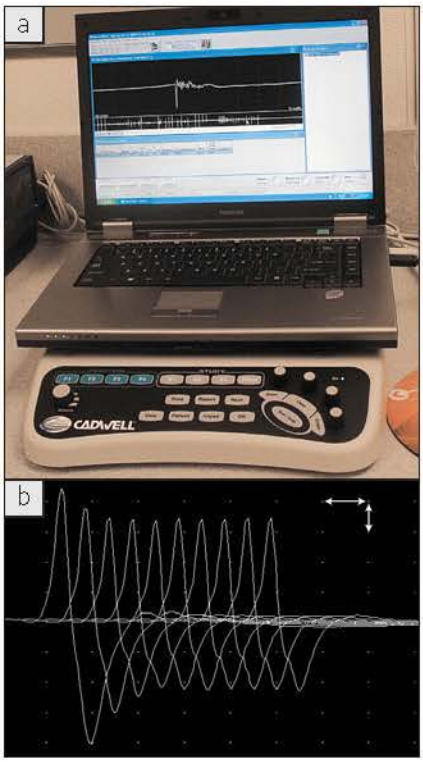
Edrophonium challenge test

The edrophonium challenge test (Tensilon test) is a diagnostic test that is relatively easy to perform and may help to establish a clinical diagnosis of AMG while the results of antibody testing are pending. Edrophonium chloride is an ultra-short-acting anticholinesterase agent that allows more ACh to be available for binding to the functional AChR present on skeletal muscle. The recommended dose is 0.1–0.2 mg/kg IV in dogs and 0.25–0.5 mg/kg IV in cats. The author recommends placement of an intravenous catheter, as this test is not without risk. Overstimulation of the AChR can produce depolarizing blockade and worsening of muscle weakness. This is known as a 'cholinergic crisis' and respiratory paralysis may result. In addition, overstimulation of the muscarinic AChR may lead to salivation, vomiting, defecation, urination, bronchoconstriction and bradycardia. Therefore, it is recommended to 'pre-treat' with atropine (0.02–0.04 mg/kg IM or SC) and be prepared to treat such a cholinergic crisis with intravenous atropine (0.02–0.04 mg/kg). Because atropine is an antimuscarinic agent, it will not have any effect on the nicotinic AChRs at these doses and therefore will not interfere with the edrophonium test. The dog should be exercised to the point of detectable weakness. The test is considered positive when a patient demonstrates marked improvement in muscle strength shortly after the administration of the edrophonium chloride. The improvement usually lasts a few minutes, after which the patient returns to its pre-treatment state. This is a subjective test and the results are not always clear and definitive. Some 'true' myasthenic patients do not respond positively to intravenous edrophonium. These patients may not have enough functional AChRs available to respond to the abundance of ACh. This is particularly the case in dogs with acute fulminating AMG. Conversely, false-positive results are possible. There can be subjective improvement in muscle strength with other NM conditions, such as polymyositis. When edrophonium chloride is not available, neostigmine methyl sulphate can be used (40 µg/kg IM or 20 µg/kg IV). This challenge test is not useful for dogs with focal AMG. Because the edrophonium challenge test is a subjective test for AMG, other diagnostic options are required for a definitive diagnosis of AMG.

Electrodiagnostic testing

Electrodiagnostic testing of the nerves and muscles is a common tool for determining the presence of NM disease. Motor and sensory nerve conduction studies are normal in patients with AMG. Electromyography studies can show normal to increased insertional activity without spontaneous myofibre discharges. Occasionally, chronic severe MG can give rise to abnormal spontaneous electrical muscle activity. Because these 'classic' electrodiagnostic tests are not specific for AMG, two additional electrodiagnostic studies are performed (**348**):

- Repetitive nerve stimulation testing in patients with AMG often reveals a decrement in the amplitude of the compound muscle action potential (CMAP). The CMAP is a summation of action potentials from numerous muscle fibres belonging to a number of motor units. A greater than 10% decrease in the amplitude and/or the area of successive CMAPs during a train of 10 stimulations at a rate of 1–3 Hz is suggestive of AMG. Unfortunately, this test lacks specificity and sensitivity and requires general anaesthesia, which might not be desirable in a critical patient.
- Single-fibre electromyography (SF-EMG) investigates NM transmission and evaluates the extent to which diseases directly affect the ability of the NM junction to synthesize or release ACh or the ability of the postsynaptic membrane to respond to ACh. When muscle action potentials are recorded from a single muscle fibre with an SF-EMG electrode, the latency from the stimulus to the response varies; this is known as jitter. Most jitter is produced by fluctuations in the time it takes for the end plate potentials at the NM junction to reach the action potential (depolarization) threshold. Jitter is a sensitive measure of the safety factor of NM transmission. It becomes increased when the safety margin is smaller than normal (or when the ratio between the depolarization threshold and the end plate potential becomes increased). MG is the most common disorder that reduces the safety factor of NM transmission. SF-EMG is the most sensitive test for diagnosing MG in humans. However, the test requires a high degree of expertise and the cost of the SF-EMG needle is substantial, therefore it is not commonly performed in veterinary medicine.



▲ 348 (a) The Cadwell Sierra Wave, a multipurpose electrodiagnostic machine that has the capability of performing single-fibre electromyography and repetitive nerve stimulation tests, which are helpful in the diagnosis of MG. (b) Supramaximal repetitive stimulation of the distal ulnar nerve (carpal stimulation) and recording from the palmar interosseous muscles in a dog with acquired myasthenia gravis. Note the decremental response in compound muscle action potential amplitudes over the first four recorded waveforms; greater than 10% (24% in this case) with low stimulation rate (3Hz in this case). The scale applies to each individual waveform, but the distance between them does not correspond to the stimulation frequency on this computerized representation. Vertical double arrow represents 2mV and horizontal double arrow represents 2ms. (Photo courtesy Nicolas Granger)

Confirmatory diagnostic tests

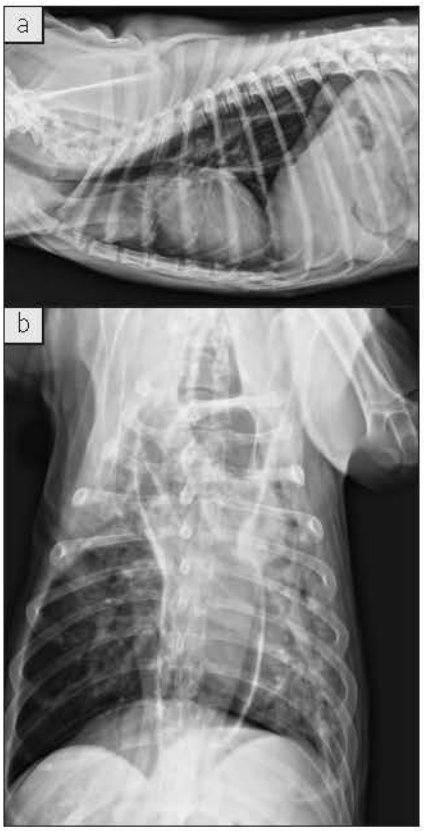
Immunocytology

Immunocytochemical staining of muscle end plates is another diagnostic test available to help diagnose AMG. Immunoglobulin localized to the end plate regions of skeletal muscle can be identified by an immunocytochemical method. The reagent used is a staphylococcal protein A (SPA) linked with horseradish peroxidase (HRPO). This reagent is incubated with fresh muscle tissue. The SPA binds to the Fc portion of the immunoglobulin and the HRPO stains the region where the binding occurs. SPA-HRPO conjugate is not specific for the antibodies against the AChR, so false positives are possible. However, a negative result will rule out a diagnosis of AMG unless the patient has received prednisone or other immunosuppressive drugs prior to testing.

Serum AChR antibody assay

The 'gold standard' diagnostic test for AMG in dogs and cats is demonstration of circulating AChR antibodies using ^{125}I-labelled α-bungarotoxin bound to native AChR in a radioimmunoassay. The assay is objective, quantitative and specific, demonstrating an autoimmune response to AChRs. Serum AChR antibody titres >0.6 nmol/l are diagnostic for AMG in dogs; titres >0.3 nmol/l are diagnostic in cats. The test detects approximately 98% of dogs with AMG. Two percent of myasthenic dogs are categorized as 'seronegative'. Several mechanisms as to why the test does not identify all affected dogs have been proposed:

- There might be a strong affinity of the antibody to the muscle end plate, resulting in undetectable amounts of antibody in the serum.
- During solubilization of the AChR for the test probe, damage to certain antigenic epitopes of the AChR can occur and the test probe might therefore fail to recognize some antigenic variations of the AChR antibodies.
- Some of the antibodies in AMG may be directed against antigenic proteins of the end plate region other than the AChR and these would not be identified by the test.
- Dogs treated with prednisone or other immunosuppressive agents for at least 7–10 days prior to testing have a decreased amount of circulating antibody, which may not be detected by the test.



▲ **349** (a) Right lateral thoracic radiograph depicting megaoesophagus and a cranial mediastinal mass (thymoma). (b) Ventrodorsal radiograph depicting megaoesophagus and severe aspiration pneumonia.

It is recommended that dogs and cats with negative titres be re-tested one month later to evaluate for seroconversion. The titres tend to be lower in focal AMG than in generalized or acute fulminating AMG, but there is no direct correlation between severity of clinical signs and the level of antibody titre in dogs.

Ancillary diagnostic tests

Thoracic radiographs should also be included in the diagnostic plan. Radiographs should be evaluated for the presence of a cranial mediastinal mass, megaoesophagus and aspiration pneumonia (**349**). The presence of aspiration should prompt collection of tracheal wash or bronchoalveolar lavage for cytology and culturing to assist in optimal antibiotic therapy. The relative oesophageal diameter is of little diagnostic value in distinguishing dogs with megaoesophagus secondary to AMG versus other causes of megaoesophagus. Therefore, other diagnostic options are needed to more definitively diagnose AMG. When megaoesophagus is suspected and not evident on radiographs, oesophagography with liquid barium or fluoroscopy may be performed, but caution must be taken as the risk of aspiration pneumonia in dogs with megaoesophagus and AMG is high. Because other autoimmune disorders such as hypothyroidism and hypoadrenocorticism have been associated with AMG, adrenal and thyroid testing are recommended in suspected myasthenics.

Congenital myasthenia gravis

Diagnosis of CMG begins with signalment, history and presenting clinical signs. In addition, these animals often display a positive response to the drophonium challenge test. The serum AChR antibody titre is normal. EMG testing is normal. Diagnosis is supported by demonstration of a decremental response with repetitive nerve stimulation, which may be reversed with administration of edrophonium chloride. Definitive diagnosis is based on demonstration of decreased AChR content in a muscle biopsy. The intercostal muscles have the highest concentration of AChR and are the muscles of choice for the test. External intercostal muscle AChR content <0.1 pmol/g tissue is suggestive of CMG (normal reference: 0.2–0.4 pmol/g tissue).

MANAGEMENT

Therapy for AMG should be tailored to the individual needs of the patient. The three main aspects of therapy for MG are anticholinesterase therapy, immunomodulatory therapy and supportive care.

Anticholinesterase therapy

Anticholinesterase therapy is the mainstay therapy for treatment of both CMG and AMG. Anticholinesterase drugs prolong the action of ACh at the NM junction by reversibly inhibiting AChE and thus enhancing NM transmission. The agent that is used most commonly is pyridostigmine bromide (1–3 mg/kg either PO or via a feeding tube q8–12h in dogs, 0.25 mg/kg q8–12h in cats). To avoid a cholinergic crisis, it is recommended to start at the low end of the dose rate, three times daily, and increase as needed. In dogs who cannot tolerate oral drugs and where a feeding tube is not available, neostigmine bromide can be administered (0.04 mg/kg IM q6h) because it has a rapid onset of effect, but shorter duration, when given parenterally than pyridostigmine. For critical animals, a constant rate intravenous infusion of pyridostigmine bromide (0.01–0.03 mg/kg/hour) may be given until oral feedings are resumed or a feeding tube is placed. Common side-effects of anticholinesterase drugs include nausea, cramps, diarrhoea, salivation and lacrimation. These may be abated with concurrent administration of atropine or administration of the drug with a meal. Overdosing with anticholinesterase drugs will lead to an excess accumulation of ACh at the NM junction, resulting in weakness as a result of depolarization and desensitization of the postsynaptic membrane. An increase in anticholinesterase medication that does not produce a dramatic increase in muscle strength should be quickly reversed in order to avoid a cholinergic crisis. The edrophonium chloride challenge test can be used to monitor treatment for dogs on pyridostigmine as well as help to differentiate between under and over-treatment. If treatment is inadequate, edrophonium chloride will provide immediate amelioration of signs of weakness, whereas in a cholinergic crisis due to over-treatment the signs will be temporarily aggravated.

Anticholinesterase agents are useful in the treatment of all forms of MG. Although they do not correct the underlying aberrant immune response, the natural course of canine AMG is to go into spontaneous remission. If an optimal response is successfully achieved and muscle strength is regained, anticholinesterase agents and supportive care may be all that is needed for treatment. However, for more refractory cases of AMG, the addition of immunomodulatory drugs is indicated.

Immunomodulatory therapy

The indications for immunomodulatory therapy are:

- Dogs with persistently elevated AChR antibody titres.
- Seropositive dogs that had a negative edrophonium chloride challenge test.
- Dogs with less than optimal response to anticholinesterase agents.
- Dogs with unacceptable side-effects relating to therapeutic anticholinesterase treatment.
- Cats seem to respond better to combined immunomodulatory and anticholinesterase treatment.
- AMG and not CMG patients, as there is no immune-mediated basis for CMG.

Corticosteroids and other immunomodulatory drugs should not be administered until the patient is stable and aspiration pneumonia, if present, has resolved.

Corticosteroids

Corticosteroids, such as prednisone, show some benefit in the treatment of human MG, but they should be used with caution in dogs with MG. The main cause of death in canine myasthenic patients is aspiration pneumonia associated with megaoesophagus, a complication not commonly seen in human patients. Prednisone is contra-indicated in these patients because it has the potential to exacerbate pneumonia. In addition, corticosteroids may exacerbate weakness in dogs with MG. The worsening of clinical signs is a direct negative effect of glucocorticoids on excitation–coupling of the contractile elements within myofibres and altered function of the ion channel of the AChR. Consequently, lower initial corticosteroid doses

(0.5 mg/kg q24h or q48h) gradually increased to higher doses (2 mg/kg q24h) in 0.5 mg/kg increments every 2–4 days have been recommended in canine AMG. Unlike dogs, exacerbation of muscle weakness may not occur as frequently in cats treated with high doses of corticosteroids. Once muscle strength has returned, the dosage of prednisone can be reduced very slowly while monitoring carefully for relapse.

Mycophenolate mofetil

Mycophenolate mofetil is a lymphocyte-specific immunosuppressive drug that has shown promise in the treatment of canine AMG. Mycophenolate mofetil's active compound, mycophenolic acid, selectively inhibits the action of the enzyme inosine monophosphate dehydrogenase, which is necessary for the *de novo* synthesis of guanosine triphosphate (GTP). A lack of GTP impairs a cell's ability to synthesize DNA, RNA, proteins and glycoproteins. Lymphocytes are preferentially targeted by mycophenolic acid, while other leucocytes, such as neutrophils and macrophages, are unaffected. Mycophenolate mofetil increases the clinical remission rate in dogs with AMG. Additionally, because of the lack of non-specific immunosuppression, it can be used safely in patients that have, or are at risk for developing, aspiration pneumonia. In a recent study, the one year mortality rate was 38% for dogs with AMG treated with pyridostigmine alone, compared with 28% for dogs treated with both pyridostigmine and mycophenolate. Mycophenolate mofetil is initially administered at a dosage of 20 mg/kg orally twice daily. After one month of therapy, the dosage is decreased to 10 mg/kg twice daily to avoid cumulative adverse gastrointestinal effects. Side-effects of mycophenolate mofetil include bone marrow suppression and cumulative gastrointestinal irritation (vomiting and diarrhoea), which occur most commonly when the initial dosage is continued for longer than one month. The cost of the drug is high and may be prohibitive in large breed dogs. Because of its promising efficacy and limited side-effects, mycophenolate mofetil should be considered in cases of AMG refractory to anticholinesterase agents alone or in all cases of AMG where megaoesophagus is present. In addition to the oral formulation, an intravenous one is available. This formulation is useful in patients in the acute setting or patients with severe megaoesophagus, where regurgitation may hinder oral administration of drugs. In a recent case series, three dogs with generalized MG and concurrent ME were treated with intravenous mycophenolate mofetil. Signs of clinical remission were evident within 48 hours. Once resolution of the ME was achieved, oral administration replaced the intravenous administration.

Azathioprine

Azathioprine is a cytotoxic antimetabolite drug that is effective in treating humans with MG. Through its active metabolite, 6-mercaptopurine, azathioprine decreases lymphocyte proliferation, with a subsequent decrease in immunoglobulin production. It is relatively specific for T lymphocytes, but can cause bone marrow suppression. Other adverse effects include gastrointestinal irritation and hepatotoxicity. These adverse effects typically resolve with reduction of drug dosage or discontinuation of therapy. The initial dosage for azathioprine in dogs is 2 mg/kg orally per day. The dosage is then tapered to an every other day regimen after the desired clinical response is achieved. Periodic (every 1–2 weeks) monitoring of the haemogram is recommended in the initial stages of therapy and every 1–2 months thereafter to monitor for bone marrow suppression. In a limited case series, four of five dogs treated with azathioprine (four dogs were concurrently treated with pyridostigmine; one was treated concurrently with prednisone) appeared to have a positive clinical response to therapy with minimal side-effects; however, the exact efficacy of this drug and its role in the treatment of canine AMG have not yet been established. A major disadvantage of this medication is the delay of 2–8 weeks before a clinical response is observed.

Cyclosporine

Cyclosporine, a calcineurin inhibitor, inhibits T-cell activation and prevents synthesis of several cytokines including interleukin-2 (IL-2). Without stimulation by IL-2, further T-cell proliferation is inhibited and cytotoxic activity is decreased. Cyclosporine is specific for lymphocytes, and minimal bone marrow suppression is noted. Side-effects include gingival hyperplasia and mild gastrointestinal upset. Based on very limited clinical data, cyclosporine at a dosage of 4 mg/kg every 12 hours might be effective in cases of AMG where anticholinesterase therapy alone fails.

Thymectomy

Surgical removal of hyperplastic thymic tissue is associated with long-term clinical improvement in humans with generalized forms of AMG. The potential benefits of thymectomy for canine MG patients is unknown; however, complete removal of thymomas has been associated with normalization of the AChR antibody titre and resolution of clinical signs. Surgical removal of a thymoma also resulted in rapid resolution of megaoesophagus in a dog with focal AMG.

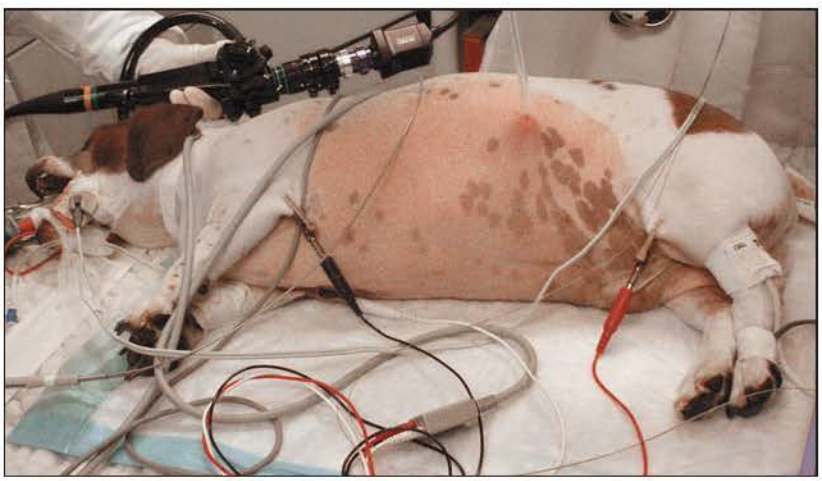
Supportive care

Supportive care and nutritional support are critical when treating a patient with MG. In those patients with normal pharyngeal and oesophageal function (i.e. without megaoesophagus), supportive care is minimal. Oral feeding can continue normally because the risk of aspiration pneumonia is low. In a patient with pharyngeal dysfunction or megaoesophagus, a nutritional plan must be devised. If the patient is able to consume food orally and is not continually regurgitating, oral feeding still might be possible. The best consistency of food varies depending on the individual and may be dry dog food, gruel or canned food. Feeding the patient in an upright position with elevated bowls, or holding the dog upright after eating, is helpful to encourage the passage of food from the oesophagus to the stomach (**350**). In patients that continually regurgitate or present with megaoesophagus and concurrent aspiration pneumonia, placement of a gastric feeding tube is strongly recommended.



▲ **350** **Keeping the dog upright for a while after feeding in a Bailey chair, as here, or similar, is necessary to reduce the potential for regurgitation. (Courtesy Roxie's MEGA Mission)**

Tubes can be placed surgically or via endoscopic guidance (percutaneous endoscopic gastrostomy tube) (**351**). In large breed patients (>25 kg body weight) the former is recommended to ensure proper placement and formation of an adequate seal with the body wall. Once a tube is in place, all feedings, water and medications should be



◀ **351** **Placement of a percutaneous endoscopic gastrostomy tube in a patient with megaoesophagus.**

given through the tube. Nothing should be allowed orally until clinical remission, including resolution of the megaoesophagus, has been achieved. Placement of a gastrostomy tube requires general anaesthesia, which may present a significant risk in some myasthenic patients. A 'low-profile' replacement gastrostomy tube can be utilized long term for added convenience. In cases of acute fulminating AMG, parenteral nutrition may be the only feasible option and should be implemented as soon as possible.

Aspiration pneumonia is a common complication related to AMG and the main cause of death in these patients. Early detection and aggressive treatment are vital for a successful outcome. Radiography, pulse oximetry, arterial blood gas monitoring, body temperature monitoring and careful auscultation allow early identification of pneumonia. Patients with aspiration pneumonia should be treated with broad-spectrum antibiotics, ideally based on culture and sensitivity results from tracheal wash specimens. In addition, respiratory supportive care, including supplemental oxygen, nebulization treatments and coupage exercises, is beneficial (**352**). Certain antibiotics (i.e. aminoglycosides, ampicillin, ciprofloxacin, erythromycin and imipenem) should be avoided because they can have potentially adverse effects on the NM junction. In cases of acute fulminating AMG, ventilatory support is usually required due to weakness of the intercostal muscles and/or diaphragm or severe aspiration pneumonia.



▶ **352** **Respiratory supportive care. (a) Patient with severe aspiration pneumonia, intubated, receiving oxygen and being monitored with pulse oximetry and a capnograph. (b) Patient with myasthenia gravis and aspiration pneumonia being treated with nasal oxygen. (c) Coupage exercises being performed on a patient with aspiration pneumonia and myasthenia gravis.**

PROGNOSIS

Overall, the prognosis for AMG is guarded. Approximately 84% of patients have megaoesophagus, and aspiration pneumonia is the main cause of death in canine patients with AMG. In dogs, the 1-year mortality rate has been reported to be as high as 60%. German Shepherd Dogs appear to have a more guarded prognosis. Because fewer cats develop megaoesophagus and aspiration pneumonia, the 1-year mortality rate for cats is only 15%. There is an inverse relationship between the concentration of AChR antibodies in cats and the prognosis. Higher concentrations are associated with more acute and severe clinical signs (acute fulminating cases have the highest AChR antibody titres), therefore this titre may be used to determine the prognosis for cats. A similarly strong correlation has not been established in dogs; however, monitoring serial AChR antibody titres in an individual is a good indicator of disease status. There is an excellent correlation between resolution of clinical signs and return of the AChR antibody titre below the normal level of 0.6 nmol/l in dogs. As long as a patient has an elevated titre, therapy should be continued despite any resolution of clinical signs. Care must be taken when evaluating serial AChR antibody titres in patients receiving immunomodulatory therapy, as false-negative results can occur. Despite the overall guarded prognosis for dogs with AMG, especially for those with aspiration pneumonia, there is a frequent occurrence of spontaneous remission among canine myasthenics. A large percentage of dogs with AMG (88.7%), regardless of the form, enter a spontaneous immune and clinical remission at an average of 6.4 months after diagnosis. Those dogs that do not enter spontaneous clinical remission are at an increased risk for developing neoplasia, including thymoma. The high incidence of spontaneous clinical remission makes it difficult to evaluate the efficacy of various treatment protocols and establish a standard of care. A similar study evaluating the natural course of the disease has not been performed in the cat.

Response to treatment of CMG is usually poor and the complete resolution of clinical signs is uncommon. Weakness is usually progressive and death commonly occurs within 1 year of age, although with treatment, some individuals might survive longer. In contrast with previously reported cases of CMG in dogs that are relentlessly progressive, spontaneous remission of clinical signs was recently reported in two Dachshunds with CMG by 6 months of age without medical therapy.

TETANUS AND BOTULISM

Jacques Penderis

INTRODUCTION

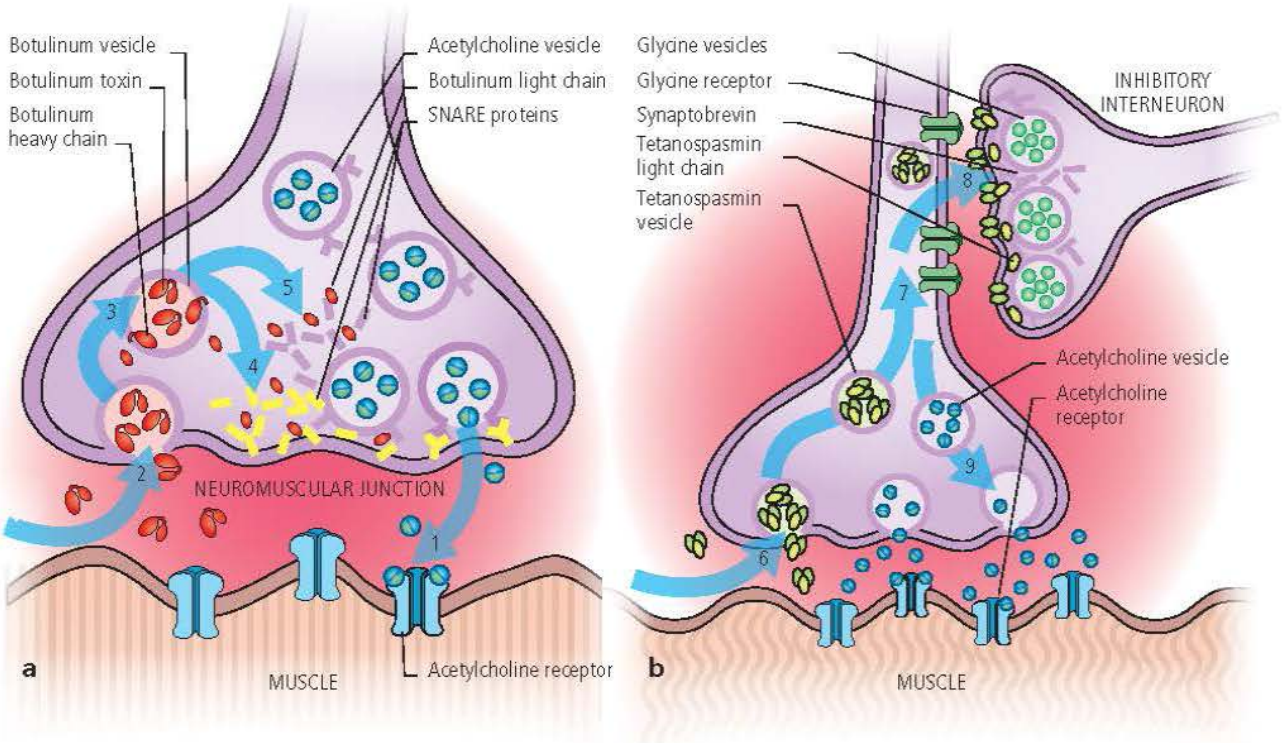
Tetanus is a disease characterized by prolonged muscle contraction (either focal or generalized). It is caused by production of the neurotoxin tetanospasmin, usually within an anaerobic wound. There are marked differences in species susceptibility, with the horse being highly susceptible, while the dog is much less susceptible (around 600 times less susceptible) and the cat even less so. Tetanospasmin (tetanus toxin) is produced by the gram-positive, obligate anaerobic bacterium *Clostridium tetani*. The toxin binds irreversibly to presynaptic sites of inhibitory neurons and recovery from the clinical signs of tetanus requires the formation of new axonal terminals. The toxin is usually degraded within the gastrointestinal tract if ingested orally.

Botulism is a neuroparalytic disease characterized by symmetrical flaccid (LMN) paralysis affecting motor and autonomic nerves and is caused by botulinum neurotoxin. Botulism occurs occasionally in dogs, most commonly secondary to dietary ingestion of preformed toxin, but has only once been demonstrated clinically in cats (although it can be produced experimentally). Botulinum toxin is the most potent known naturally-occurring acute toxin and is most commonly produced by the gram-positive, anaerobic, spore-forming bacterium *Clostridium botulinum*. Toxin within *C. botulinum* spores are heat resistant and the toxin is resistant to low pH and is not denatured in the stomach. Botulinum toxin produced by different strains of *C. botulinum* have different antigenic properties (with seven recognized, of which type C is the most common in dogs). Different strains of toxin require different antitoxins.

AETIOLOGY/PATHOPHYSIOLOGY

Tetanus

Tetanus is seen with moderate frequency in veterinary patients and is caused by the neurotoxin tetanospasmin, formed by the gram-positive, obligate anaerobe *C. tetani*. *C. tetani* is found around the world and *C. tetani* spores are ubiquitous in the environment, in particular in soil, faeces and dust. The spores are highly resistant (including to heat and some disinfectants) and survive for prolonged periods in the environment, in particular in soil with high moisture and organic content. Following a contaminated wound, the spores gain entry to the body and convert into the vegetative form. This process is made more likely in the presence of concurrent local tissue infection, abscessation, necrosis or a foreign body. However, in a substantial number of cases no evidence of a wound can be identified. Following germination into the vegetative form, local production of tetanus toxins occurs, in particular the neurotoxin tetanospasmin. Tetanospasmin is usually degraded within the gastrointestinal tract if orally ingested and does not cross the placenta. There are a variety of different strains of *C. tetani*, but in all these strains the tetanospasmin toxin produced has the same antigenic properties and therefore a single antitoxin is effective against tetanospasmin produced by all strains of *C. tetani*.



▲ 353 **The mechanism of action of (a) botulism and (b) tetanus neurotoxins. (1) Normal acetylcholine release at the NM junction. (2) The botulinum toxin is haematogenously transported from the gut to the axon terminal where it is absorbed via endocytosis. (3) The heavy chain of the toxin releases the light chain into the terminal cytoplasm, where it cleaves specific SNARE proteins (4, 5) required for fusion of acetylcholine vesicles to the presynaptic membrane, thus preventing their exocytosis. In contrast, the tetanus neurotoxin usually enters the bloodstream through a wound. It, too, attaches to the presynaptic membrane (6), but is transported back through the axon into the CNS (7). The toxin then binds to inhibitory interneurons and, as with botulism, the light chain is freed. This targets the vesicle-associated membrane protein synaptobrevin, preventing the release of the inhibitory neurotransmitters GABA and glycine (8) and leading to uncontrolled release of acetylcholine (9).**

The toxin is spread haematogenously (or, in some cases, locally) and binds preferentially to NM junctions, from where it undergoes retrograde axonal transport to the neuronal cell body (**353**). From there the toxin spreads via synaptic junctions to adjacent motor and autonomic neurons. Tetanospasmin cleaves synaptobrevin, one of the vesicle-associated membrane proteins required for neurotransmitter release. The main effect of tetanospasmin is on inhibitory pathways (in particular interneurons inhibiting alpha motor neurons), where it prevents the release of glycine and GABA, resulting in failure to inhibit motor reflexes. The consequence of this is dramatically increased muscle tone and rigidity. Early involvement of the facial muscles ('risus sardonicus' and trismus ['lockjaw']) reflects the relatively short axonal pathways of neurons innervating these muscles (**354**). All muscles are affected in generalized tetanus, but the clinical finding of extensor limb rigidity and trismus reflects the greater strength of the extensor muscle groups and the muscles that close the jaw, in comparison with the flexor muscle groups and muscles that open the jaw. The most common form of tetanus is generalized tetanus, where the entire body is affected, but localized tetanus may also occur in a single limb in close proximity to a wound.

Involvement of the autonomic nervous system tends to occur later in the disease course, but may continue for 1–2 weeks. The exact mechanism is unknown, but the most widely accepted theory involves impairment of inhibitory circuits in the autonomic nervous system.

The clinical signs vary and reflect overstimulation of either the sympathetic or parasympathetic nervous system. Dogs with naturally occurring tetanus appear to have more parasympathetic overactivity with fewer sympathetic signs. Increased parasympathetic tone commonly results in bradycardia, bradyarrhythmias and hypotension. Increased sympathetic tone results in vasoconstriction, tachycardia and hypertension. In some cases, episodes of excessive catecholamine release occur secondary to adrenal stimulation, resulting in episodes of tachycardia and hypertension, contrasted with periods of bradycardia and hypotension.

Binding of tetanospasmin to neurons is irreversible and recovery requires the generation of new nerve terminals. This explains the slow recovery in these cases.



▲ 354 Generalized tetanus in an English Springer Spaniel with a nail bed infection. Generalized tetanus is characterized by dramatically increased muscle tone of the limbs, body and head. The facial musculature demonstrates 'risus sardonicus', which is characterized by the ears drawn together, lips drawn back and wrinkling of the forehead.

Botulism

Botulism is relatively uncommon in veterinary patients and the majority of cases can be linked to eating animal or bird carcasses, food that has spoilt or food that has been stored inappropriately in anaerobic conditions, allowing the growth of bacteria. Botulinum toxin is usually produced by *C. botulinum* bacteria, but may also be produced by some strains of *C. baratii* and *C. butyricum*. *C. botulinum* bacteria are a heterogeneous group of gram-positive, anaerobic, spore forming, rod bacteria, which are all characterized by the production of botulinum toxin. Botulinum toxins produced by different *C. botulinum* bacteria have different antigenic properties, allowing them to be subdivided into seven distinct strains (types A, B, C1, D, E, F and G). All reported canine cases to date have been caused by type C toxin, with the exception of two cases reported from Senegal caused by type D toxin. Naturally occurring botulism has only been reported once to date in cats, where a group of cats were fed pelican carrion; however, the disease has been experimentally produced in cats. Botulism is reported in man and a variety of other animals, with different antigenic strains responsible for disease in different species. Different strain types produce identical clinical signs, but strain type is important as strain-specific antiserum is required for treatment. Botulism in man has been reported secondary to types A, B, E and F. Type C is also the most common strain in other animals, although strain D is sometimes also seen in cattle, strain B is reported in horses and strains A and E occur in birds and mink.

C. botulinum is found worldwide and is a relatively ubiquitous bacterium, present in the soil, marine and freshwater sediments and the gastrointestinal tracts of mammals and fish. *C. botulinum* is capable of producing spores and these are resistant to heat, light, desiccation, many chemical agents and radiation. Under anaerobic conditions, combined with a high organic nutrient environment, the bacterium produces botulinum toxin as it grows. Vegetative cells contain higher levels of toxin than spores; toxin is only released following cell or spore lysis. However, the toxin contained within spores is resistant to heat denaturation. In most veterinary cases, botulism occurs following ingestion of preformed toxin in food that has spoilt (either food that has been poorly stored or carrion), but in occasional cases botulism may occur following colonization of anaerobic tissues by *C. botulinum*, with local toxin production. There is also

some anecdotal evidence to suggest that in a multiple dog outbreak of botulism from a kennel environment, dogs that did not have access to the contaminated diet may still have developed botulism, presumably by ingestion of botulism toxin through coprophagia. Botulism secondary to ingestion of preformed toxin in spoilt food is also the most common form in man, but two other clinical variants occur in man: infant botulism and infant-like botulism. Both of these forms are due to in-vivo botulinum toxin production following intestinal colonization with botulinum toxin-forming clostridial bacteria. Intestinal colonization causing botulism has been reported in a young dog.

Following cell or spore lysis in spoilt food (carrion is the most common source in dogs) the toxin is released and binds with other protein complexes to form progenitor toxins. These progenitor toxins are extremely stable, particularly at low pH, and pass through the stomach into the small intestine, where the toxin is released and absorbed.

The toxin is absorbed from the small intestine by endocytosis, enters the lymphatic system and from there the bloodstream. Botulinum toxin in the blood stream binds rapidly and with extremely high affinity to presynaptic peripheral nerve terminals, affecting the limb, trunk and head muscles. Differences in toxin binding affinity explain the differences in species susceptibility. The process of neuronal binding comprises: (1) binding with neuronal cell surface receptors, (2) endosomal internalization of the toxin, (3) membrane translocation and, finally, (4) modification of target SNARE proteins required for exocytosis of ACh at the NM junction. Botulinum toxin binds rapidly and irreversibly to the neuronal cell surface receptors and once it has been internalized it is no longer vulnerable to antitoxin. At the NM junction, SNARE proteins are required for docking and fusion of the synaptic vesicles with the presynaptic cell membrane. Targeting of the SNARE proteins by botulinum toxin prevents presynaptic release of ACh at the NM junction, resulting in flaccid (LMN) paralysis and evidence of autonomic nervous system dysfunction. Botulinum toxin inhibits ACh release at the NM junction following a motor action potential, as well as spontaneous ACh release (**353**).

CLINICAL PRESENTATION

Tetanus

Two forms of tetanus are described in domestic animals: localized tetanus and generalized tetanus. Localized tetanus, where limb rigidity is seen close to a wound, is less common. Generalized tetanus results from haematogenous spread of the tetanospasmin toxin. Clinical signs first become apparent 5–10 days after a wound in which growth of *C. tetani* bacteria has occurred, and this delay may explain why there is often no wound apparent when a case is presented with clinical tetanus. Wounds closer to the head are associated with more rapid onset and more commonly present as generalized tetanus than wounds distally on the limbs. Generalized tetanus may also occur following a recent ovariohysterectomy in dogs. Localized tetanus with spasticity of one hindlimb and scoliosis has been reported in cats following ovariohysterectomy. Cats are more resistant to tetanus, resulting in a decreased incidence and longer time to onset (up to 3 weeks); however, when it does occur in cats it is usually associated with larger wounds producing larger amounts of toxin.

Localized tetanus

Localized tetanus is uncommon in human patients, but is more common in cats and dogs due to their increased innate resistance. Local muscular stiffness and rigidity develop in a single limb or the paraspinal muscles in association with a wound or in the hindlimbs in association with infection of the reproductive tract of females or following ovariohysterectomy. The stiffness progressively develops from the distal extremity to affect the entire limb, before affecting the opposite limb and then the entire body, with the head the last region to be affected. In some cases of localized tetanus there is no progression of the clinical signs.

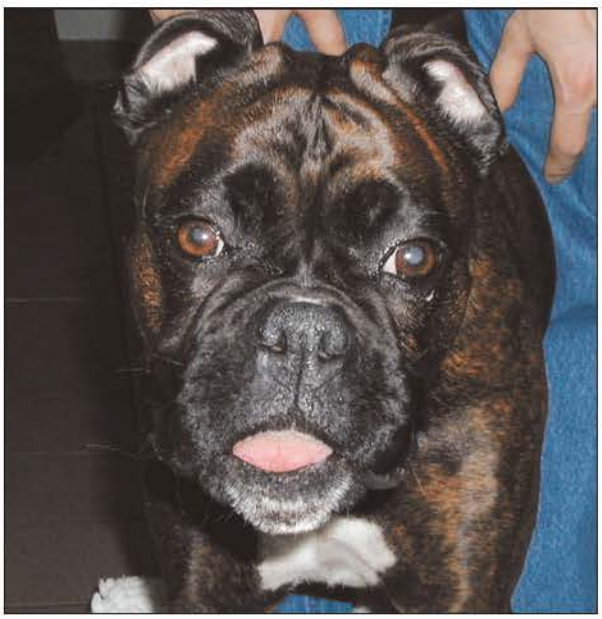
Generalized tetanus

In generalized tetanus the head and neck musculature is affected first, followed by the body and limbs. Affected animals have a stiff and stilted gait with difficulty standing up or lying down due to the muscular stiffness. The limbs are usually held in extension and the tail may be

held out straight or curved dorsally. Muscle stretch reflexes are often exaggerated and may go into persistent clonus following stimulation. The CNs are affected relatively early in generalized tetanus, with the combination of trismus ('lockjaw') and the typical facial expression ('risus sardonicus'), which comprises the ears drawn together, lips drawn back and wrinkling of the forehead (**355, 356**). In addition, there may be protrusion of the third eyelids, enophthalmos due to contraction of the retractor bulbi muscles and miosis. Autonomic instability may be evident in more severe cases as tachycardia or bradycardia, respiratory compromise and dysphagia. Urine retention/inability to void can also be noted as a result of a hypertonic urethral sphincter requiring continual or intermittent urinary catheterization.

Muscle tetany occurs in response to auditory, visual or tactile stimuli and may be generalized, resulting in opisthotonus or even progress to generalized seizures. Consciousness is not impaired (unless seizures develop) and the tetany may be extremely painful, with animals exhibiting distress during the episodes. The presence of trismus makes prehension of food difficult; more severe cases may have evidence of dysphagia and regurgitation.

The effect of autonomic dysfunction means that gastrointestinal and urinary dysfunction are common. The constant muscle contractions may result in hyperthermia. Death is usually the consequence of cardiac or respiratory failure. Respiratory failure usually arises due to laryngospasm, rigidity of respiratory muscles or suppression of the respiratory centre in the brainstem.



▲ **355** Reflecting their shorter axonal length and therefore the decreased distance tetanus toxin needs to be transported retrograde, the cranial nerves are affected relatively early in generalized tetanus with the combination of trismus ('lockjaw') and the typical facial expression ('risus sardonicus'), which comprises the ears drawn together, lips drawn back and wrinkling of the forehead.



▲ **356** In contrast to tetanus, other conditions causing contraction or abnormally increased tone of the cranial muscles, as in this left-sided facial nerve contraction secondary to facial nerve irritation, do not result in the characteristic 'risus sardonicus' expression.

Botulism

Botulism is characterized by an afebrile, flaccid (LMN) paralysis with additional involvement of the autonomic nervous system. The onset and severity of clinical signs are dependent on the total dose of toxin ingested and the individual susceptibility of the animal. Clinical signs typically develop rapidly within 12 hours (but can be up to 6 days) following ingestion of the toxin. The more rapidly the clinical signs develop, the more severe the disease tends to be. Affected animals develop a progressive and symmetrical paresis, progressing to flaccid paralysis that typically first becomes evident in the hindlimbs before extending to the forelimbs. Voluntary control of the tail wag is often preserved. Reflexes and muscle tone are decreased to absent, which is consistent with an LMN lesion.

In severe cases the respiratory musculature may be affected with decreased abdominal tone and primary diaphragmatic respiration. The diaphragm is more resistant to botulism toxin and is only affected in very severe cases. Death may result from paralysis of the respiratory muscles or be secondary to aspiration pneumonia and complications resulting from prolonged recumbency.

Sensory function, including pain perception, and level of consciousness are unaffected. Distinct from other causes of diffuse LMN disease, in botulism there is more frequently additional evidence of CN deficits (e.g. facial nerve paralysis, depressed gag reflex, decreased jaw tone, reduced vocalization and megaoesophagus), as well as (in some cases) evidence of dysfunction of the cholinergic neurons of the autonomic nervous system. The cholinergic signs include alterations of heart rate (increased or decreased), pupil changes (mydriasis with depressed pupillary light reflexes), keratoconjunctivitis sicca, urinary retention and constipation.

DIFFERENTIAL DIAGNOSIS

Tetanus

The main differential diagnoses for generalized tetanus include bacterial meningoencephalitis, epileptic seizures (however, these are usually episodic in nature and normally resolve with administration of diazepam), strychnine poisoning, hypocalcaemic tetany and severe generalized sepsis. Masticatory muscle myositis should be considered in focal tetanus affecting the head. In endemic regions, cerebral canine babesiosis and rabies should also be considered.

Botulism

The main differential diagnoses for flaccid (LMN) paralysis include acute fulminating MG and acute polyradiculoneuritis. The following diseases may also need to be considered as part of the differential diagnosis list (either as less common differential diagnoses, or in endemic regions): tick bite paralysis (tick paralysis); neuroparalytic snake envenomation; post-vaccination polyradiculoneuritis; organophosphate toxicity; blue-green algae (anatoxins) and green algae (charatoxin); black widow spider envenomation (the latter stages of envenomation are characterized by flaccid paralysis, although this is preceded by muscle fasciculation); and accidental administration of NM blocking agents (e.g. vecuronium and succinylcholine). Rabies should be considered in endemic regions, particularly if CN deficits are dominant.

DIAGNOSIS

Tetanus

Diagnosis of tetanus is based on the typical clinical presentation of persistent muscle rigidity or tetany (focal or generalized) and, in generalized tetanus, the additional involvement of the face ('risus sardonicus' and trismus ['lock-jaw']) and autonomic instability (bradyarrhythmias or tachyarrhythmias). A recent history of a wound or neutering of a female dog would support the diagnosis, but often a wound is not identified.

To further substantiate the diagnosis, routine biochemical and haematological testing is usually normal, excluding other causes; however, elevation of muscle enzymes may occur in response to prolonged muscle contracture. If available, electromyography may be used to confirm the presence of sustained muscle depolarization in anaesthetized animals. In most animals the muscle contraction is reduced with anaesthesia, but usually does not totally resolve. Bacterial isolation is usually unrewarding and is not helpful in most cases. *C. tetani* is an obligate anaerobe and therefore culture must be performed under strict anaerobic conditions. Serological testing can be performed to demonstrate a titre against tetanospasmin toxin; however, this is not generally useful in the clinical setting and is probably only useful in unusual cases of focal tetanus. Control animal samples would need to be submitted with the suspect case.

Botulism

Diagnosis of botulism is primarily based on the history and suggestive clinical presentation. Due to the dietary origin of the toxin, multiple cases may occur within the same group of animals and there may be a history of exposure to carrion. In many cases of botulism in domestic animals and human patients the underlying organism is not identified. In part this relates to the ubiquitous nature of the *C. botulinum* in the environment, and culture of food or environmental samples is therefore usually of little use.

Routine investigation

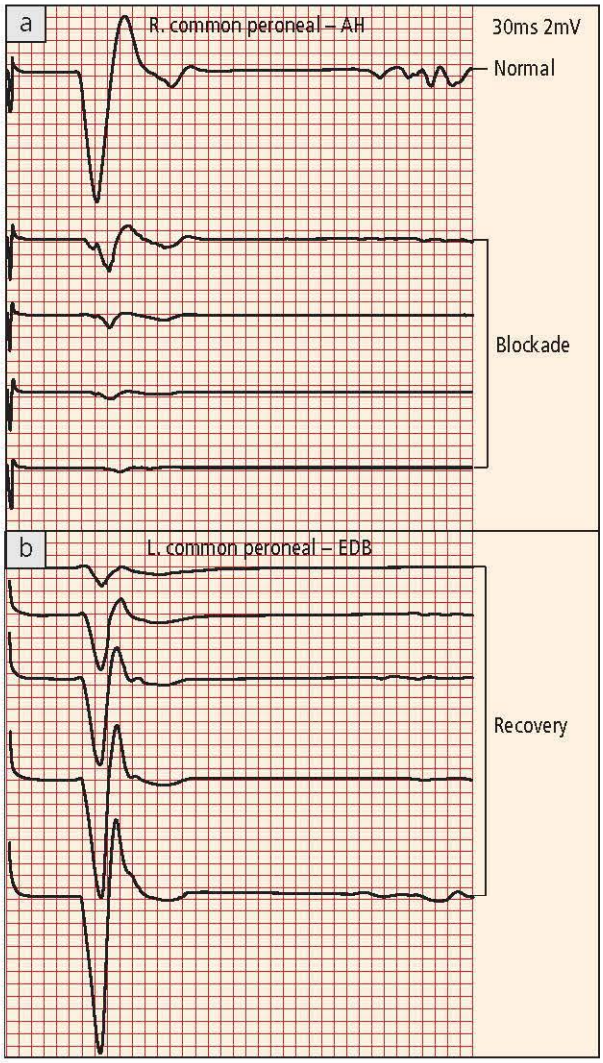
The results of routine investigation (including routine haematology, biochemistry and CSF analysis) are usually normal or reflect secondary complications of recumbency and paralysis. Conscious thoracic radiography should be performed to assess for evidence of megaoesophagus and secondary aspiration pneumonia.

Demonstration of botulinum toxin

Definitive diagnosis is based on the demonstration of botulinum toxin early in the course of the disease, either in blood (10 ml of serum should be collected) or gastrointestinal tract contents (50 g of faeces, vomitus or food sample should be collected). The more rapidly the sample is collected after the onset, the higher the likelihood of confirming the diagnosis. In human patients, samples collected within 24 hours of onset are positive in over 50% of cases, but this drops to less than 25% in samples collected 3 days after onset. It is essential to discuss the diagnostic sample requirements with the laboratory performing the investigation. The samples should be refrigerated, but not frozen (freezing affects the vegetative form of *C. botulinum*, but does not affect the toxin). The sample should be labelled as a biological hazard, particularly as people are considerably more susceptible than dogs or cats to botulism toxin. The gold standard test is a mouse biological assay, in which serum or a sample of faeces, vomitus or food is inoculated into two groups of mice, one group of which is protected with antitoxin. The development of clinical signs consistent with botulism in the unprotected mice provides confirmation. However, the test is expensive and requires live animals and is therefore not often performed in veterinary patients. Alternatives to the mouse biological assay include ELISAs and PCR to detect botulism toxin in food, but many of these tests are still being validated at the time if writing.

Isolation of *C. botulinum*

As has already been discussed, culture from food or the environment is not helpful, but culture of the organism from a patient's faeces or gastric contents may be very helpful in supporting the diagnosis. *C. botulinum* can be successfully cultured from the faeces or gastric contents in around 60% of human patients.



◀ **357** **(a) EMG of vecuronium-induced neuromuscular block demonstrating the typical electrodiagnostic features of decrease in transmission at the neuromuscular junction, similar to that seen in botulism. Following stimulation of the common peroneal nerve, intravenous vecuronium administration results in marked reduction of compound motor action potential amplitude during motor nerve conduction, in the presence of normal nerve conduction velocity and no evidence of temporal dispersion of the compound motor action potential. The recordings were performed prior to vecuronium administration (top trace) and intermittently over the 2 minutes immediately afterwards. The reduction in amplitude reflects the decrease in transmission at the neuromuscular junction. (b) Recovery from vecuronium-induced neuromuscular block similar to that seen in botulism. The increasing amplitude of the resulting compound motor action potential following stimulation of a motor nerve indicates recovery of neuromuscular junction transmission. AH = abductor halluci; EDB = extensor digitorum brevis.**

Electromyography and nerve conduction studies

Electrodiagnostic evaluation of muscle and nerve function may assist in the diagnosis, but is not definitive. The typical electrodiagnostic feature of botulism is marked reduction in compound motor action potential amplitude during motor nerve conduction, in the presence of normal nerve conduction velocity and no evidence of temporal dispersion of the compound motor action potential (**357**). The reduction in amplitude reflects the decrease in transmission at the NM junction. In addition to the reduction in amplitude, there are some reports of identification of mild fibrillation potentials and increased insertional activity on electromyography after prolonged periods of paralysis (around 2 weeks), followed by positive sharp waves on recovery, and subtly decreased motor nerve conduction velocities in some canine patients, but these findings are not reliably present and consideration should be given to an alternative cause. Repetitive nerve stimulation at low frequency (less than 5 Hz) may produce a small decrement in compound motor action potentials; rapid stimulation (50 Hz) are likely to produce an increment in successive compound motor action potentials, and this increment is highly supportive of botulism. Evidence of increment on high-frequency stimulation may only be evident in a few muscle groups, despite multiple muscle groups being weak or paralysed.

MANAGEMENT

Tetanus

The management of generalized tetanus requires intensive treatment with frequent monitoring. Binding of tetanospasmin to neurons is irreversible and recovery requires the generation of new nerve terminals. For this reason, improvement is usually only evident after about one week of treatment. Sudden death can occur due to respiratory failure or aspiration. Facilities for respiratory support should be available and animals should be closely monitored for respiratory distress. General monitoring should include vital signs, arterial blood gases (especially $PaCO_2$ levels), pulse oximetry and respiratory rate and effort.

Supportive care

The most important aspect of the treatment of tetanus cases is the quality of the supportive care. Patients should be kept in a dark and quiet area and any stimulation minimized in order to reduce the risk of precipitating seizures or severe muscular contractions. Foam ear plugs (or pieces of cotton wool) should be placed in the ears to limit stimulation by sound. If the ears are kept occluded for a prolonged period (more than a couple of days), there is the likelihood of developing a marked moist otitis externa and the ears should be regularly cleaned and allowed to dry, with the animal sedated with midazolam or diazepam during the procedure. Because affected animals are recumbent, they should be kept on soft bedding and kept clean and dry to avoid urine and faecal scald.

Maintaining adequate nutrition and fluid intake is an important part of management. Weight loss is a significant problem due to the inability to open the mouth, dysphagia, abnormal gastrointestinal function due to autonomic dysfunction and the increased metabolic demands associated with the increased muscle tone. Animals are also at risk of dysphagia and gastro-oesophageal reflux, with a concomitant risk of aspiration pneumonia. Consideration should be given to placing a gastrostomy or oesophagostomy tube. If that is not possible, although less ideal, animals can be carefully fed with soft food or a nasogastric tube can be placed; however, in all cases there is still the risk of gastro-oesophageal reflux and aspiration.

Other supportive care considerations in tetanus cases reflect the prolonged recumbency and the muscular rigidity and stiffness that these patients experience. These include decubital ulcers from prolonged recumbency, aspiration pneumonia due to the dysphagia and recumbency, respiratory impairment, urinary and faecal retention (which may require bladder catheterization and enemas), hyperthermia from the sustained muscle contraction and acute renal failure secondary to rhabdomyolysis following a prolonged tetany.

Antitoxin administration

Free circulating tetanus toxin should be neutralized with tetanus antitoxin. Available tetanus antitoxins include antitetanus equine serum and human tetanus immunoglobulin (HTIG). Bound tetanus toxin is not affected by antitoxin. All animals with acute tetanus should have the antitoxin administered and this should be performed prior to wound débridement, as wound débridement results in further tetanus toxin release. The route of administration affects the availability of the antitoxin, with subcutaneously administered tetanus antitoxin taking 2–3 days to reach therapeutic levels. Intravenous administration is therefore preferable. Following administration of tetanus antitoxin, effective therapeutic levels are maintained for at least 2 weeks and repeated injections are not required (and are associated with a greater risk of adverse reactions). Adverse reactions to tetanus antitoxin administration are of concern, in particular anaphylaxis, and this is more likely to occur following intravenous administration or repeated injections.

In order to limit the potential for anaphylaxis, a test dose of 0.1–0.2 ml is administered intradermally or subcutaneously prior to administration of the full dose, and the injection site monitored for 30 minutes. The development of a wheal or other reaction at the injection site indicates risk of an adverse reaction. If there is no evidence of an adverse reaction, the full dose can be administered. There is little consensus on the correct dose of tetanus antitoxin, with a total dose of 5,000–10,000 units of HTIG recommended in human patients. The dose of antitetanus equine serum is 100–1,000 units/kg (with a maximum of 20,000 units), preferably given as an intravenous bolus over 30 minutes, but it can also be administered subcutaneously or intramuscularly. In focal tetanus, local injection of a total dose



▲ **358** (a) A female intact English Springer Spaniel with generalized tetanus secondary to mastitis. Generalized tetanus is frequently associated with a recent ovariohysterectomy, sepsis of the female reproductive tract or mastitis. (b) Examination of the mammary glands confirmed them to be hot and painful, with discoloured milk indicative of mastitis. The identification and resolution of an infectious focus are associated with a better prognosis in dogs with generalized tetanus.

of 1,000 units in the proximal affected limb has been reported to be effective. Epinephrine should be available in case of anaphylaxis and if there is concern about an adverse reaction, glucocorticoids and antihistamine can be administered prior to injection of the antitoxin.

There is some evidence to suggest that intrathecal administration of a lower dose (as low as 1% of the intravenous dose; 1–10 units/kg), in addition to the intravenous dose, is beneficial in dogs with generalized tetanus. The intrathecal administration of antitoxin means that it does not need to cross the blood–brain barrier and there is a suggestion that it may partially neutralize CNS-bound toxin. However, intrathecal administration is no longer recommended in human practice because a number of studies and meta-analyses have shown that it has no benefit over parenteral administration.

Wound débridement

Following the administration of tetanus antitoxin, any identifiable wound should be thoroughly cleaned, foreign material removed and necrotic tissue débrided. It is important to look for evidence of nail bed infections and sepsis elsewhere, including mastitis and reproductive tract infections (**358**). The identification and débridement of a wound result in an improved prognosis. Wound débridement most likely would require general anaesthesia; hydrogen peroxide can be used to flush the wound in order to reduce the anaerobic bacterial load.

Antimicrobial therapy

A wide range of antibiotics are effective against *C. tetani*, with metronidazole (10–15 mg/kg IV q8h [dog] and q12h [cat]) being the antibiotic of choice. A variety of other antibiotics are viable alternatives, including erythromycin, tetracyclines, chloramphenicol, clindamycin and amoxicillin–clavulanate. In all cases the antibiotic therapy is continued for at least 10 days. There is some debate regarding the effectiveness of penicillin in cases of generalized tetanus, with many texts recommending the use of penicillin G at a dose of 20,000–100,000 units/kg slow IV or IM q8–12h. However, one randomized trial in human patients demonstrated a higher mortality in patients treated with penicillin than in those treated with metronidazole (24% vs 7%). Metronidazole may also be a better choice because it penetrates tissue with vascular compromise, including abscesses, more effectively.

Control of muscle rigidity (or tetany) and seizures

Muscle tetany, muscular rigidity and seizures require management with sedation. There are a large variety of agents that have been and can be used, but benzodiazepines are the initial treatment of choice as a continuous intravenous infusion. Either diazepam (IV bolus of 0.5–1.0 mg/kg or as a continuous IV infusion at a starting dose of 0.2 mg/kg/hour, titrated upwards to effect) or midazolam (IV bolus of 0.2–0.3 mg/kg or as a continuous IV infusion at a starting dose of 0.3 mg/kg, titrated upwards to effect) can be used, usually at higher doses than required for control of SE and titrated to effect.

The benzodiazepines are usually combined with phenothiazines in order to decrease hyperexcitability, again titrated to effect as intermittent injections. Chlorpromazine (0.2–10 mg/kg IV as required or, in dogs, a total oral dose of 5–10 mg) is the agent of choice, although other phenothiazines, including acepromazine (0.01–0.06 mg/kg IV, 0.01–0.25 mg/kg IM or SC, 1–3 mg/kg PO) and methotrimeprazine (0.5–1.0 mg/kg IV), are also effective. Chlorpromazine is effective and does not potentiate seizures in tetanus, but is not effective in other conditions associated with increased muscle tone.

If midazolam or diazepam is not effective in controlling the seizures (in those animals demonstrating seizures), longer-acting agents, in particular phenobarbital, can be used. Doses of barbiturates that suppress respiration should be avoided, as should other drugs that may suppress respiration. Propofol is also effective, but doses sufficient to cause muscle relaxation require ventilatory support and are not feasible for the length of management that is required.

Other medications that may be considered include morphine, dantrolene, methocarbamol, baclofen and magnesium sulphate. Despite the risk of respiratory depression, morphine can be effective in alleviating muscle tetany and rigidity due to a central action that reduces the effect of tetanospasmin. It is also useful in alleviating the effects of excessive catecholamine release. The muscle relaxant dantrolene has been used successfully in a few human patients, but its use is limited by cost and it may result in respiratory depression. Methocarbamol is a centrally acting muscle relaxant that can be used at a dosage of 20–45 mg/kg PO q8h. As methocarbamol is a CNS depressant, additive depression may occur when it is given with other CNS depressants. Baclofen, a structural analogue of GABA, has demonstrated a dramatic response in some human patients when administered intrathecally. Following intrathecal administration, baclofen inhibits neuronal transmission in the spinal cord, but it is associated with a significant risk of respiratory depression. Baclofen can also be administered orally, after which it is rapidly and well absorbed. Doses recommended are 1 mg/kg PO q8h up to a maximum of 5–10 mg. This medication can cause vomiting, depression and vocalization in some dogs and should be used with care. Magnesium sulphate has been recommended in humans for control of muscle tetany in severe tetanus. Magnesium plays a crucial role in neurotransmission and excitability. Its dosage (0.2 mEq/kg/hour CRI) has unfortunately not been established for animals with tetanus and is extrapolated from human reports. Magnesium dosing should be titrated to reduce rigidity to an acceptable level without causing respiratory depression. ECG and systemic BP monitoring are advised while establishing the dose of magnesium due to the associated risks of bradycardia and hypotension. Serum magnesium concentration should be maintained between 2 and 4 mmol/l.

In cases where the muscle tetany and rigidity are completely refractory to diazepam, the NM blocking agent atracurium or vecuronium can be used as a 'final resort', but this requires mechanical ventilation, which is usually not feasible in most veterinary patients.

Control of autonomic dysfunction

One of the more important causes of mortality in severe, generalized tetanus is cardiovascular failure secondary to involvement of the autonomic nervous system. The clinical signs of autonomic dysfunction are usually only evident in severe tetanus and usually resolve once animals start to improve and, in most cases, are effectively controlled by sedation. One of the main problems is that

of tachyarrhythmias, but bradyarrhythmias and sinus arrest may result from overstimulation of the parasympathetic system. Tachyarrhythmias most likely result from elevated catecholamine levels and a direct effect of tetanus toxin on the myocardium. Bradycardia is probably due to a direct effect of tetanus toxin on the vagal nucleus.

The first step in the management of autonomic dysfunction is to sedate the animal. Morphine as part of the sedative protocol is effective in decreasing catecholamine release. Other medications that are frequently used in human patients include clonidine (α2-adrenergic agonist) and magnesium (with is particularly effective in reducing autonomic overstimulation by blocking catecholamine release and reducing receptor sensitivity to catecholamines). Treatment with atropine or glycopyrolate is usually effective in reversing bradyarrhythmias.

Analgesia

Analgesics are recommended to address the pain associated with constant muscle rigidity or tetany. (For further details, refer to Chapter 30.)

Botulism

The treatment of botulism is largely supportive until new functional NM junctions have formed. Because of the requirement for prolonged supportive care and the potential for respiratory failure, hospitalization and frequent monitoring of animals are required. Respiratory failure is the main cause of death and usually develops relatively early in the disease, but a delayed onset of up to 7 days after first presentation may occur. In more severe cases, monitoring of respiratory function is important and respiratory failure may occur without preceding evidence of increased respiratory effort, respiratory rate or desaturation. As an indication of patients at risk of respiratory failure, serial measurements of respiratory function should be performed, although these are not widely available in veterinary patients. In human patients this is best assessed by serial determination of forced vital capacity or static inspiratory pressure. A decrease in static inspiratory pressure of 15–20% indicates that a patient is likely to require mechanical respiratory support. (Refer to Chapter 2 for further details on the management of compromised respiration.)

Supportive care

Supportive care represents the mainstay of treatment in botulism, in particular the avoidance of problems associated with prolonged recumbency. This involves bladder management (including prevention of retention cystitis), avoiding the development of pressure sores, access to food and water, cleanliness, support while patients return to normal exercise and physical therapy. In more severe cases, respiratory support may also be required. In cases that have recently presented and where toxin may still be present within the gastrointestinal tract, an attempt should be made to remove the material, taking care to avoid aspiration pneumonia. This may include using gastric lavage, enemas and cathartics.

Bladder management is important, as recumbent animals will tend to retain urine and may develop retention cystitis; the bladder should be kept as empty as possible to minimize the residual urine volume, either through support for urination, manual expression, intermittent catheterization or indwelling closed collection systems. Intermittent catheterization is associated with the lowest incidence of urinary tract infection, followed by manual expression and finally indwelling closed urinary collection systems.

All recumbent patients should be maintained on soft bedding and turned frequently in order to avoid the development of pressure sores. Physical therapy (massage and passive range of joint movement) will also help to maintain joint movement. The animal should also be kept clean in order to avoid urine and faecal scald and contamination of any pressure sores with faecal material. (Refer to Chapter 32 for further details on nursing care of the emergency neurological patient.)

Recumbent animals are usually unable to reach their food or water bowls, therefore maintaining daily fluid and caloric requirements is important. Care should be taken during oral feeding, particularly if dysphagia is present, as aspiration pneumonia is a risk. The use of feeding tubes and parenteral fluids should be considered.

Antibiotics may be required for secondary infections; however, they should generally be avoided, unless necessary, because of the possibility of altering the intestinal microflora and risking overgrowth with *C. botulinum*. If antibiotics are required, then those that may impair NM transmission should be avoided (in particular the

aminoglycosides, but also lincomycin, penicillamine, polymyxins and tetracyclines). Ophthalmic preparations may be necessary to protect the cornea due to paralysis of the eyelids and potentially reduced tear production.

Antitoxin administration

Antitoxin administration is currently the only specific therapy for botulism. Antitoxin is only effective in limiting the severity of the clinical signs if administered early in the disease course. Antitoxin administration will not reverse established weakness or paralysis, therefore it should be performed early in the disease course before the toxin has irreversibly bound to the nerve terminals. Most canine cases are due to type C botulism and the human trivalent antitoxin acts against types A, B and E, therefore the available antitoxin is not effective. If type C antitoxin is available, anaphylaxis and other hypersensitivity reactions are a potential risk. A small subcutaneous or intradermal test dose should therefore be administered first. Human botulism immune globulin is available and has been shown to be effective in reducing the severity and duration of disease in one of the human forms of botulism, namely infant botulism, but this is unlikely to be effective in dogs as it is not targeted against type C botulism.

Wound débridement in botulism

Most cases of botulism are due to ingestion of preformed toxin, but, less commonly, cases of wound-associated botulism with local production of botulism toxin can occur. In these cases management comprises wound débridement with concurrent antibiotic therapy. Effective antibiotics include benzyl penicillin and metronidazole. Antibiotics are contraindicated in food-acquired botulism unless there are secondary infections. Ideally, wound débridement is performed after antitoxin administration, but as human trivalent antitoxin only acts against types A, B and E botulism, this may not be effective.

PROGNOSIS

Tetanus

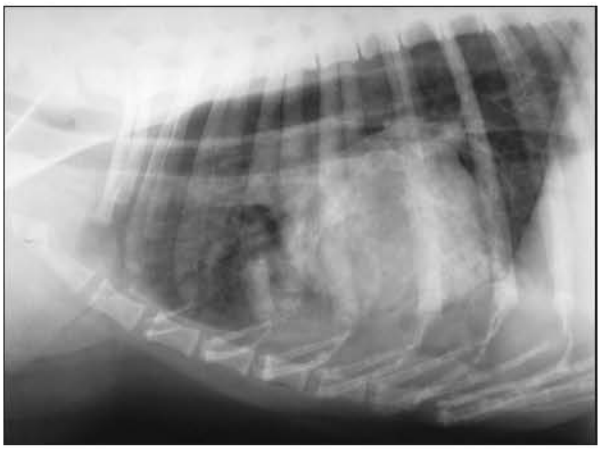
The prognosis for recovery from tetanus is dependent on the presenting severity and whether the animal is demonstrating progression. Tetanus toxin binds irreversibly to axonal terminals, resulting in disinhibition and muscular rigidity or tetany. Recovery is dependent on the synthesis of new pre-synaptic components and their transport to the distal axon, typically leading to a 2 week delay before signs of clinical improvement.

There is a grading scale for determining the prognosis in human patients, but due to the infrequency of canine and feline cases this is less useful. Localized tetanus is less common than generalized tetanus, but is associated with lower mortality and more rapid recovery. In human patients (where localized tetanus is less common than in canines and felines) the mortality associated with localized tetanus is approximately 1%. A recent retrospective study identified a significant association between younger age and development of more severe clinical signs and an inverse relationship between development of severe clinical signs (including autonomic disturbance) and survival.

In generalized tetanus the owners should be made aware of the costs of treatment, particularly as dogs will only start to demonstrate an improvement after about a week of therapy. Dogs that are unable to stand or walk without support, demonstrating opisthotonus or demonstrating seizures all have a poor prognosis for recovery.

Botulism

Animals with botulism have the potential for complete recovery with no long-term deficits if they can be supported through the period of flaccid paralysis. Despite apparent full recovery, muscle weakness may still be present for up to 1 year after recovery. The overall mortality in human patients with botulism is approximately 7–10%, but this is doubled in patients over



▲ **359** Lateral thoracic radiograph demonstrating megaoesophagus in a dog with evidence of severe secondary aspiration pneumonia. Aspiration is a risk factor in both tetanus and botulism due to the dysphagia present in both conditions, but particulaly in botulism where there is usually a concomitant megaoesophagus. The presence of aspiration pneumonia is associated with a poor prognosis in both conditions.

60 years of age. There are substantial costs associated with the duration of nursing required and the owner should be made aware of these at the outset.

The more rapid the disease onset the more severe the disease tends to be, therefore the worse the prognosis. Different muscle groups have different susceptibility to disease and this is reflected in the temporal progression of the disease as it develops and the reversal of these clinical signs as the animal recovers. The duration of disease is approximately 2–3 weeks and respiratory, CN, neck and forelimb function tends to return first.

One of the primary causes of death in severe cases is respiratory failure or secondary aspiration pneumonia (**359**). The more severe the disease (particularly with involvement of the respiratory muscles) the worse the prognosis. The prognosis is also worse in animals with pre-existing respiratory disease. The development of secondary problems associated with prolonged paralysis or recumbency, in particular aspiration pneumonia, is associated with a worse prognosis.

INTRACRANIAL NEOPLASIA AND SECONDARY PATHOLOGICAL EFFECTS

John Rossmeisl & Theresa Pancotto

INTRODUCTION

Primary brain tumours (PBTs) are neoplasms arising from the constitutive parenchymal tissues of the CNS. The most common PBTs in veterinary medicine are of mesodermal (meningiomas) or neuroectodermal (astrocytomas, oligodendrogliomas and choroid plexus tumours) origin. Astrocytomas, oligodendrogliomas and oligoastrocytomas (mixed gliomas) are the most common tumours arising in intra-axial locations in the brain and they cannot be differentiated with antemortem imaging techniques. These types of PBT are collectively and clinically referred to as gliomas.

Secondary brain tumours (SBTs) are neoplasms that haematogenously metastasize to the brain parenchyma from a distant site in the body, or compress or invade neural tissue by local extension from an anatomical site in proximity to the brain (e.g. nasal, orbital, osseous tumours of the skull, pituitary tumours). The prevalence of SBTs has been shown to be higher than that of PBTs in necropsy-based canine studies, with haemangiosarcomas, pituitary tumours and carcinomas being most common. CNS lymphoma can rarely occur as a PBT, but is more commonly seen as an SBT in association with multicentric disease.

ICP is generated from the sum total volumetric contributions from all resident tissues enclosed in the calvarium, namely the brain parenchyma, blood and CSF. The CPP is the mean arterial blood pressure less the ICP. The CPP is the driving force behind maintenance of CBF, which is the volume of blood coursing through the intracranial circulatory bed per unit time. CBF must be preserved within physiological ranges in order to meet the minimal oxygen and nutritional requirements of the brain.

The Monro–Kellie doctrine describes the relationships between pressure and volume within a closed, non-expansile system, such as the osseous calvarium. It stipulates that an increase in the volume of one of the constituents requires a compensatory decrease in another in order to maintain pressure–volume homeostasis. In the case of intracranial neoplasia, the volume of the brain parenchyma is increased by the presence of the tumour, which necessitates decreases in intracranial intravascular and CSF volumes in order to maintain the ICP within physiological ranges. This response is termed intracranial compliance, and its adaptive abilities are blunted as the ICP continues to rise (see also page 363).

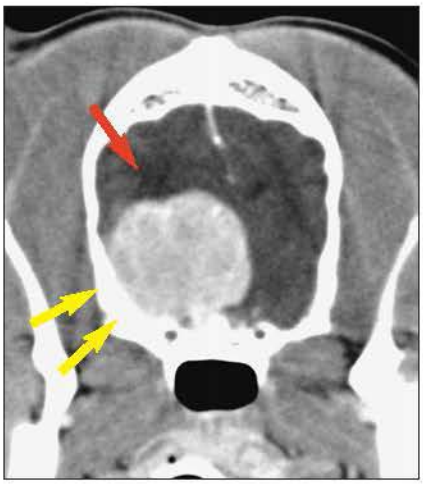
Histopathological examination of neoplastic tissue is the only method by which intracranial neoplasms can be definitively diagnosed.

AETIOLOGY/PATHOPHYSIOLOGY

Acute and often severe clinical neurological deterioration associated with PBTs and SBTs necessitating emergency treatment can usually be attributed to one of several pathophysiological alterations including: (1) neural dysfunction induced by the presence of the neoplastic mass; (2) uncompensated intracranial hypertension; (3) paraneoplastic mechanisms; and (4) drop metastases.

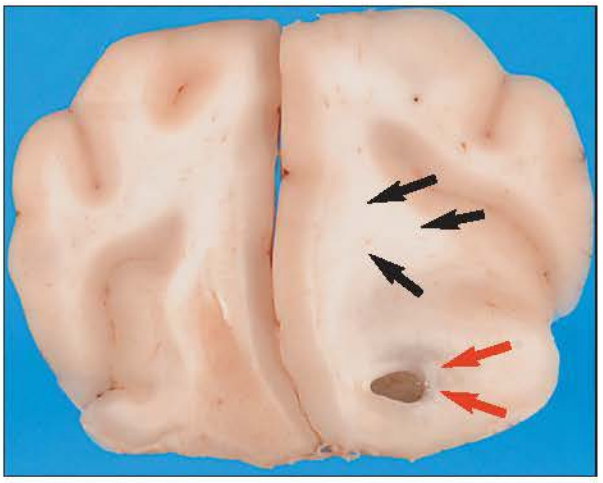
Tumour-associated brain dysfunction

Damage to neurons, glia and vascular elements can occur directly as a result of the mechanical effects of the tumour on parenchymal tissues or the subsequent inflammatory response that is generated as a result of the tumour itself. Neurons and glia in proximity to mass lesions can become dysfunctional via direct physical destruction, through multiple disturbances (synthesis, release, recycling) in neurotransmitter-mediated cellular signalling and through vascular impairment. In the early stages of tumour growth, compensatory autoregulatory mechanisms, such as shifting of CSF into the spinal subarachnoid space and decreased CSF production, are effective and ICP is maintained within physiological ranges



▲360 Axial/transverse post-contrast CT scan demonstrating a large, markedly enhancing, extra-axial mass lesion in the ventrolateral aspect of the right cerebral hemisphere. Hyperostosis of the calvarium overlying the mass (yellow arrows) can be seen when compared with the contralateral side. Peritumoural oedema is visible as the hypoattenuating region in the white matter dorsal to the mass (red arrow). Mass effect is manifested as lateral ventricular compression and a falx cerebri shift to the left. The histopathological diagnosis was a grade I, transitional meningioma.

▼ 361 Gross necropsy specimen from a 6-year-old mixed breed dog with a high-grade (grade III) oligoastrocytoma of the right fronto-olfactory lobes (red arrows). Note the midline shift and white matter oedema (black arrows) in the right cerebrum.



according to the principles of the Monro–Kellie doctrine. With slowly growing neoplasms, pressure–volume homeostatic regulatory mechanisms can remain intact despite large tumour volumes and significant mass effect (**360**). In these cases, clinical signs of neurological dysfunction are focal and referable to the neuroanatomical origin of the neoplasm. With progressive increases in tumour volume and the resultant secondary pathophysiological changes, autoregulatory mechanisms become overwhelmed and exponential and deleterious elevations in ICP occur. This results in uncompensated intracranial hypertension and dangerous decreases in CPP.

Uncompensated intracranial hypertension

Intracranial hypertension is the final pathophysiological common denominator underlying many of the mechanisms of brain injury induced by the presence of an intracranial neoplasm. Acute and catastrophic clinical deterioration due to intracranial hypertension is usually caused by accumulation of brain oedema (**361**), obstructive hydrocephalus, abnormalities of CBF (ischaemia or haemorrhage), physical displacement of intracranial parenchymal structures (**360, 362**) or combinations of these mechanisms.

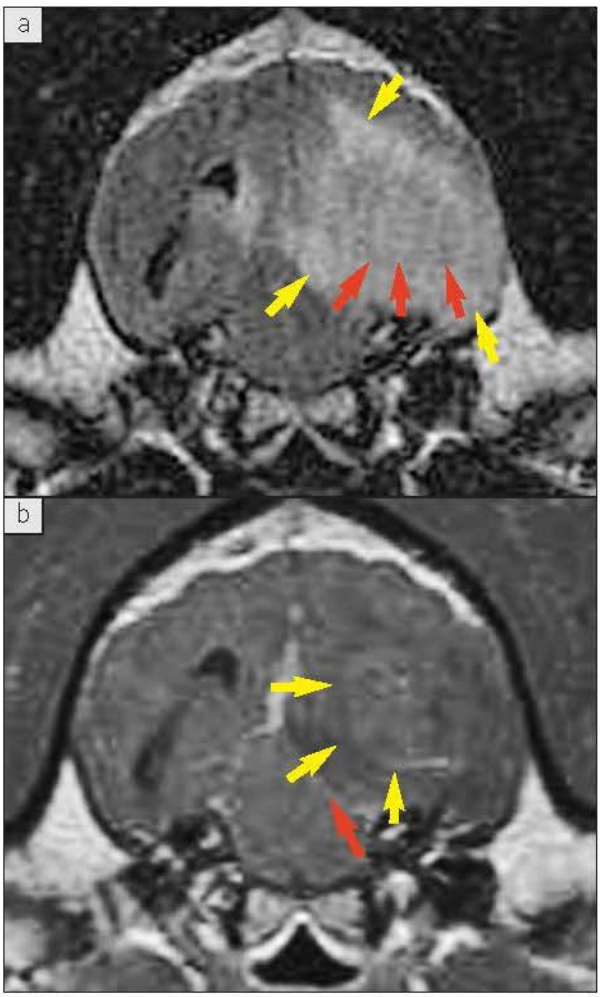
There are three main types of brain oedema that can often coexist in animals with brain disease: vasogenic, cytotoxic and interstitial.

- Vasogenic oedema is common in animals with intracranial neoplasms and results from physical or functional disruption of the vascular endothelium. Studies of multiple tumour types in humans and animals have shown that intratumoural neovasculature can be morphologically and functionally abnormal, e.g. lacking endothelium, having large endothelial fenestrations, or overexpressing receptors for pro-angiogenic proteins and vascular permeability factors such as vascular endothelial growth factor (VEGF). VEGF and its receptors are overexpressed in canine intracranial neoplasms, such as meningiomas, astrocytomas and oligodendrogliomas. These pathological alterations in vascular permeability factors may contribute to the oedema-forming potential of certain tumour types. Rostrotentorial meningiomas and high-grade gliomas are often associated with significant vasogenic oedema, which will often accumulate along subcortical white matter tracts (**360, 361, 363**).

▶ 362 Dorsal planar, post-contrast T1-weighted MR image from a dog with seizures from a multifocal intracranial choroid plexus carcinoma. Both lateral ventricles contain uniformly contrast-enhancing masses, and a falx cerebri shift is present towards the right of the midline.



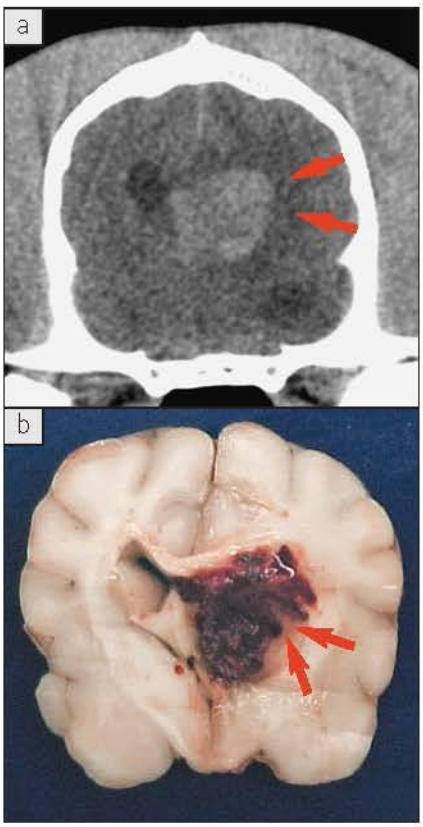
▶ 363 (a) Transverse T2-weighted FLAIR MRI scan at the level of the mesencephalon from a dog with an anaplastic (grade III) oligodendroglioma presented for stupor and decerebrate rigidity. An elliptical, poorly marginated and heterogeneously iso- to hyperintense mass lesion is present in the left cerebral hemisphere (red arrows), surrounded by a hyperintense rim compatible with oedema (yellow arrows). The mass obliterates the left lateral ventricle and causes a falx cerebri shift to the right. Periventricular oedema is also present as hyperintensity located in the dorsomedial aspect of the right lateral ventricle. (b) Transverse post-contrast T1-weighted image obtained at the same level as 363a. The mass demonstrates mild, heterogeneous contrast enhancement, particularly at its periphery (yellow arrows). The rim of peritumoural oedema appears hypointense. A left unilateral transtentorial brain herniation is also more apparent, resulting in compression of the mesencephalon (red arrow).





▲ **364** Transverse post-contrast CT scan demonstrating a well-demarcated, markedly enhancing, choroid plexus papilloma in the interventricular foramen, causing enlargement of the lateral ventricles (obstructive hydrocephalus).

- Cytotoxic oedema occurs when there is failure of the Na^+/K^+ ATPase pumps to extrude intracellular sodium, leading to an intracellular accumulation of water. It is usually due to cellular energy substrate deficiency from ischaemia/hypoxia, hypoglycaemia or excitotoxicity, or from toxins that interfere with cellular metabolism, such as reactive oxygen species and nitric oxide. Progressive distension of the cell eventually leads to cellular lysis and death. Grey matter is preferentially affected, as this tissue is more metabolically active and quantitatively contains more Na^+/K^+ ATPase pumps per unit area than white matter.
- Interstitial oedema often accompanies obstructive hydrocephalus. Obstructive hydrocephalus can result from compression of any segment of the ventricular system by the presence of an intracranial mass, intraventricular haemorrhage or ventricular occlusion by a drop metastasis that impedes CSF flow pathways. Areas of normal narrowing of the ventricular system are predisposed to obstruction by intracranial tumours, including the mesencephalic aqueduct and interventricular foramen. Tumours that form in intraventricular locations, such as choroid plexus tumours, ependymomas and meningiomas, are often associated with obstructive hydrocephalus (**364**). In obstructed regions, as the intraventricular pressure rises, compartmentalized CSF will cross ventricular walls, resulting in periventricular interstitial brain oedema (**363a**).

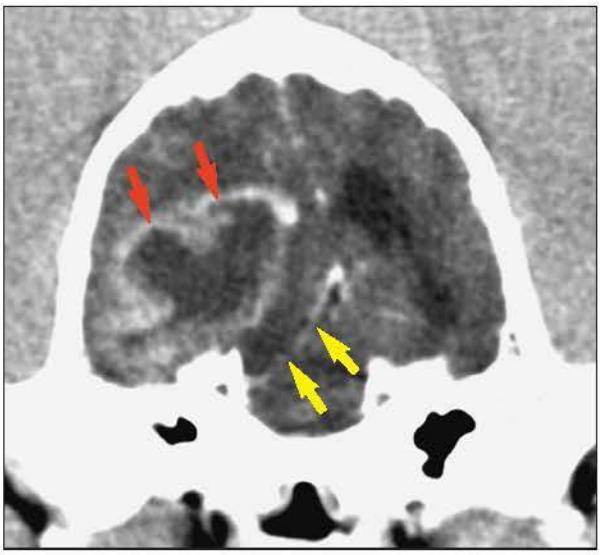


◀ **365** (a) Transverse CT scan from a dog with status epilepticus, demonstrating a hyperattenuating intraventricular mass lesion within the left lateral ventricle, with hypoattenuating perilesional white matter oedema (arrows) and mass effect. (b) Gross necropsy specimen obtained from approximately the same level as the CT scan, revealing intraventricular haemorrhage and haematoma associated with choroid plexus carcinoma (arrows).

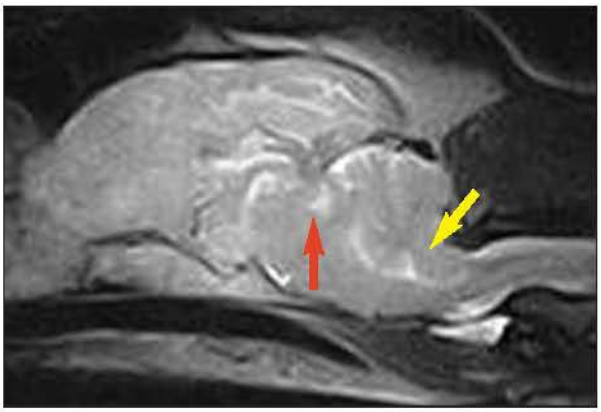
Neoplastic erosion into, or compression of, brain vasculature can result in intracranial haemorrhage, intravascular neoplastic embolization or ischaemic brain infarction. High-grade gliomas and choroid plexus carcinoma, whose phenotypes are often defined by significant neovascular proliferation, may haemorrhage spontaneously in intratumoural, intraventricular, subarachnoid, epidural or intraparenchymal locations. Haemorrhage can result in acute neurological deterioration if it is severe enough to cause a mass effect or obstructive hydrocephalus from resultant haematoma formation (**365**). Ischaemic infarctions will result in the evolution of cytotoxic and vasogenic brain oedema, which will further exacerbate intracranial hypertension; however, this is dependent on whether the infarct is lacunar or territorial in nature (see Chapter 17).

Brain herniations are the terminal effects of intracranial hypertension. Three types of spontaneous brain herniation are commonly observed in patients with intracranial neoplasms. These are subfalcine, transtentorial and foramenal herniation (**360, 366, 367**).

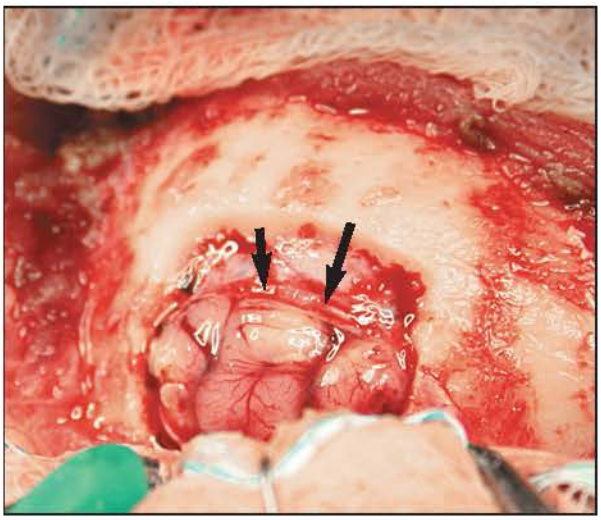
- Subfalcine. A marked increase in volume of one cerebral hemisphere from tumour mass, oedema, haemorrhage or ventricular obstruction can result in subfalcine herniation, which is medial displacement of the affected cerebral hemisphere under the falx cerebri. Subfalcine herniations are commonly associated with, or preceded by, diagnostic imaging evidence of a falx or midline 'shift'. In the axial (transverse) and dorsal imaging planes, a falcine shift appears as a displacement of the normally sagittally located falx cerebri away from the hemisphere containing the mass, across the midline towards the contralateral cerebral hemisphere (**360, 361, 362**).
- Transtentorial herniation is the unilateral or bilateral displacement of the cerebral hemisphere(s) beneath the tentorium cerebelli, resulting in compression of the mesencephalon and/or rostral cerebellum (**363, 366**).
- Foramenal herniation (**367**) is characterized by shifting of the caudoventral aspect of the cerebellar vermis through the foramen magnum, with secondary compression of the underlying medulla.



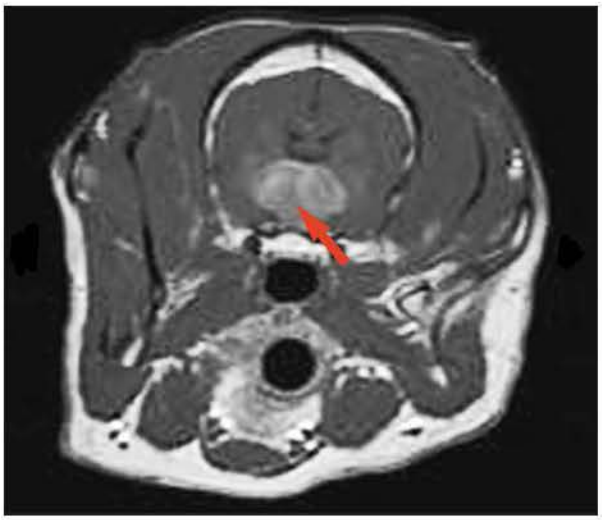
▲ **366** Transverse post-contrast CT scan at the level of the mesencephalon of an 8-year-old Boston Terrier dog with a right forebrain anatomical diagnosis. A ring-enhancing mass (red arrows) is present in the right occipital lobe of the cerebrum. Significant mass effect is visible as a falx cerebri shift, compression of the mesencephalon by a transtentorial brain herniation (yellow arrows) with resultant shifting of the mesencephalic aqueduct to the left of midline. The histopathological diagnosis was glioblastoma multiforme (grade IV astrocytoma).



▲ **367** Sagittal, T2-weighted MR image from a comatose dog demonstrating foramenal herniation (yellow arrow). A caudal transtentorial herniation can also be seen (red arrow).



▲ 368 Intraoperative herniation of the brain parenchyma overlying a cerebral glioma through a parietotemporal craniectomy defect following durotomy. The arrows delineate the dorsal limits of the durotomy.



▲ 369 Transverse post-contrast T1-weighted MR image of a dog with seizures and pituitary-dependent hyperadrenocorticism associated with a pituitary macroadenoma (arrow).

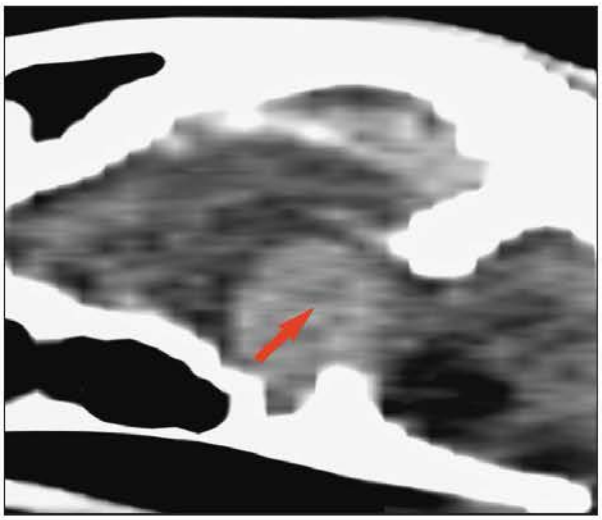
The clinical signs associated with brain herniations are discussed in the clinical presentation section below. Subfalcine herniations may be clinically occult. The brain parenchyma may also herniate through craniectomy defects intraoperatively (**368**) or postoperatively.

Paraneoplastic syndromes

A paraneoplastic syndrome is an alteration in the structure or function of an organ that is anatomically distant from the site of the tumour. With respect to the brain, paraneoplastic syndromes are primarily the result of the distant effects of hormones produced autonomously by functional and neoplastic pituitary glands (**369**) or from hormonal deficiency secondary to neoplastic destruction of the pituitary gland, both of which lead to systemic target organ dysfunction. It is important to recognize paraneoplastic syndromes as potential premonitory signs of underlying intracranial neoplasia. In addition, the clinical effects of these hormonal abnormalities on the quality of life of affected animals and their owners can be more devastating than the actual effects of the tumour.

The most common examples of paraneoplastic syndromes associated with functional pituitary tumours include dermatological and metabolic changes that frequently accompany canine and feline pituitary-dependent hyperadrenocorticism (PDH) and feline acromegaly (**370, 371**). Cats with functional pituitary tumours are more likely than dogs to present as an emergency for extraneural signs. This can be attributable to sepsis related to cutaneous wounds resulting from skin fragility in cases of PDH (**371**) or metabolic crises associated with concurrent insulin-resistant diabetes mellitus (PDH and acromegaly). Neurological emergencies associated with PDH can be the result of tumour-induced neuronal dysfunction or from vascular encephalopathy, as hypercoagulability and hypertension are well-recognized complications of PDH predisposing to cerebrovascular accidents (see Chapter 17).

Less common examples of paraneoplastic pituitary syndromes include acquired central diabetes insipidus (CDI) and pituitary apoplexy. Animals with CDI resulting from neoplastic infiltration of the pituitary from a



▲ 370 Sagittal, post-contrast CT scan from a cat with chronic, insulin-resistant diabetes mellitus and an acute onset of circling to the right. The cat had a markedly elevated serum IGF-1 concentration and the pituitary macrotumour visible in this image (arrow) is consistent with a diagnosis of feline acromegaly.



▲ 371 Cutaneous wound in the flank of a cat that occurred during routine restraint for venipuncture. The cat had insulin-resistant diabetes mellitus, a dexamethasone suppression test consistent with hyperadrenocorticism and a pituitary macrotumour.

variety of PBTs and SBTs have been reported. These cases typically have histories of severe polyuria/polydipsia and hyposthenuria resulting from antidiuretic hormone deficiency preceding the development of neurological signs. Acute and severe alterations in consciousness accompanied by seizures in animals with acquired CDI are the result of hypertonic dehydration and hypernatraemia. These neurological crises are often precipitated by restricted access to water, which can be iatrogenic on the part of the owner in an attempt to palliate severe polyuria and perceived urinary incontinence. Pituitary apoplexy is the peracute onset of neurological impairment associated with infarction or haemorrhage of a pituitary tumour, and has been rarely described in dogs. Associated neurological signs can be non-specific (e.g. depression and behaviour change), but can also include visual deficits and seizures. In some instances the initial neurological dysfunction is mild enough that owners do not seek veterinary attention, and animals present as an emergency from the delayed effects of partial or complete hypopituitarism and secondary empty sella syndrome (**372,** next page). Secondary empty sella syndrome is the term used to describe a secondary reduction in pituitary volume due to infarction, pituitary surgery or irradiation, cystic pituitary lesions, compression from adjacent intrasellar neoplasms or following chemotherapy for pituitary tumours. In these instances, presenting signs are usually attributable to a secondary hypoadrenocortical crisis.

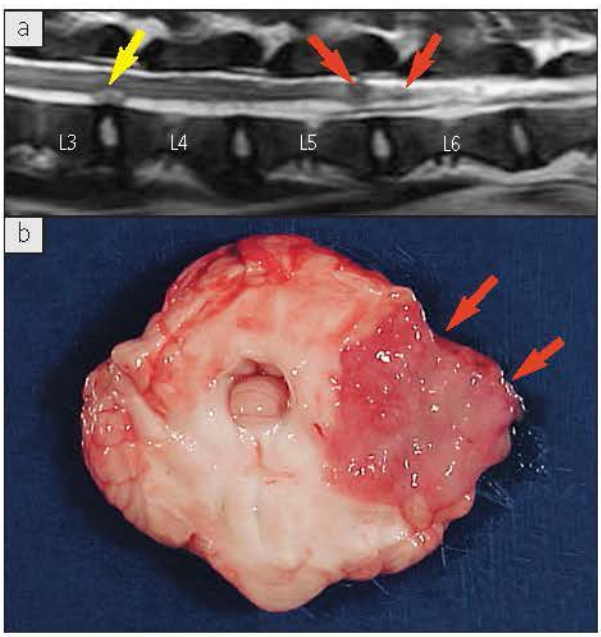
Drop metastases

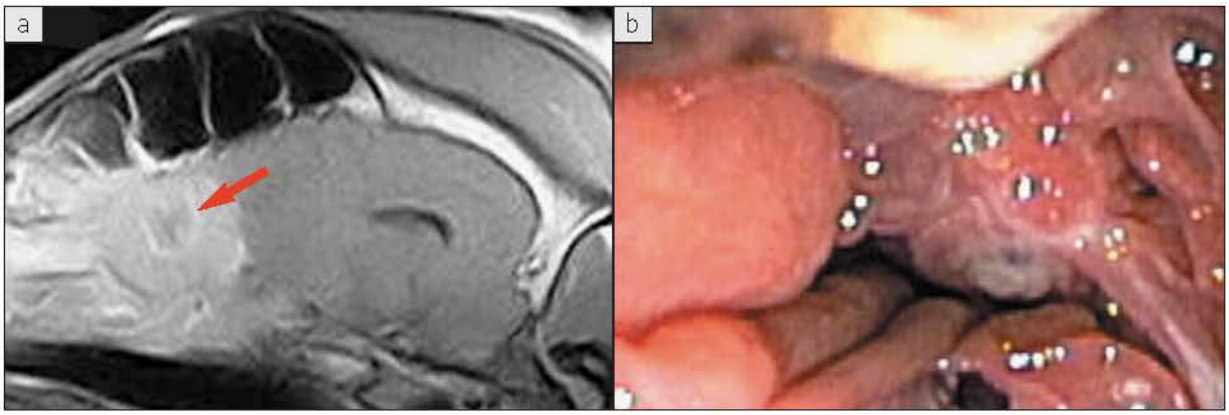
Intracranial or spinal intradural, extramedullary tumour foci developing at sites remote from a primary neoplasm are called drop metastases. The mechanism of metastasis is exfoliation of neoplastic cells into the subarachnoid space. Choroid plexus tumours, ependymomas and meningiomas have been rarely associated with drop metastases, but virtually any intracranial tumour can metastasize in this manner if it is contiguous with the subarachnoid space. The development of drop metastases may also be a result of seeding of the subarachnoid space during surgical removal of intracranial tumours.



◀ **372** Transverse FLAIR (a), T2-weighted (b) and sagittal T1-weighted (c) MR images from a dog with previous clinical and biochemical evidence of pituitary-dependent hyperadrenocorticism successfully managed long term with trilostane. A CT scan of the brain performed 8 months previously revealed a normal pituitary gland. The dog presented for stupor, collapse, vomiting and diarrhoea associated with a hypoadreno-cortical crisis. The images demonstrate a fluid-filled region occupying the central portion of the pituitary (arrows). The presumptive diagnosis was secondary empty sella syndrome secondary to infarction of the pituitary gland.

▼ **373** (a) Sagittal T2-weighted MR image from the lumbar spine of a 5-year-old Golden Retriever with flaccid paraparesis and central vestibular signs. Multifocal, heterogeneously iso- (yellow arrow) to hypointense (red arrows) appearing, intradural-extramedullary drop metastases from an intracranial choroid plexus carcinoma are present in the L3/L4 and L5/L6 regions. (b) Gross necropsy specimen obtained at the level of the cerebellum from the same dog. The friable pink mass (arrows) at the right cerebellopontomedullary angle is a choroid plexus carcinoma.





▲ 374 (a) Parasagittal, post-contrast, T1-weighted MR image from a dog presented for epistaxis, stertorous respiration and seizures. A uniformly contrast enhancing mass lesion (arrow) is noted in the nasal cavity and fronto-olfactory regions of the cerebrum. (b) Rhinoscopic photograph of the nasal portion of the mass; the histopathological diagnosis was a poorly differentiated nasal carcinoma.

Clinical signs associated with drop metastases are reflective of the location(s) of the metastases, and may result in a multifocal CNS neurolocalization (**373**). Affected animals have also been reported with acute, severe spinal cord dysfunction attributed to drop metastases whose intracranial tumours have been clinically occult.

CLINICAL PRESENTATION

If the neoplasm and any of its associated pathophysiological effects are confined to a focal region of the brain, the clinical signs should localize to that area during the neurological examination. Although the majority of PBTs occur as solitary intracranial masses, the clinical presentation is often consistent with a multifocal intracranial disease process as a result of tumour-associated pathophysiological alterations, especially in animals with uncompensated intracranial hypertension. Locally invasive SBTs may also cause neurological multifocal signs secondary to bacterial meningoencephalitis, resulting from a breach of the integrity of the calvarium, especially seen with tumours arising from the oral and nasal cavities (**374**), or bullae.

Seizures and behavioural changes are very commonly reported clinical abnormalities with prosencephalic neoplasms. A brain tumour should be considered as a differential diagnosis in any dog or cat ≥5 years of age with an onset of seizures. Historical evidence of seizure activity or behavioural change may be the only manifestation of an underlying brain tumour, as rostral prosencephalic neoplasms can often be associated with normal interictal neurological examinations. Central vestibular signs are common in animals with caudotentorial intracranial tumours.

Primary complaints in cases presented as an emergency in association with intracranial neoplasms are typically associated with acute and profound alterations in consciousness, status epilepticus or cluster seizures, head and body postural abnormalities or progressive gait and balance disturbances. When interpreted in conjunction with a complete neurological examination, head and body postural abnormalities and gait disturbances may provide additional neurolocalizing information, but in many instances they are reflective of progressive, secondary pathophysiological sequelae such as brain herniation. Evaluation of neurological dysfunction and therapeutic progress are achieved through serial performance of the MGCS in stuporous or comatose animals in which routine components of the neurological examination cannot be interpreted. The components and interpretation of the MGCS are discussed elsewhere in this book (see Chapter 20).

Performance of a complete and systematic physical examination, including a fundoscopic evaluation, is also indicated to identify deleterious systemic consequences of intracranial hypertension, extraneural sources of primary tumours in dogs with an SBT, or other significant concurrent diseases. Intracranial hypertension may result in visible papilloedema. Massive, acute rises in ICP have been associated with the development of the cerebral ischaemic response. The cerebral ischaemic response may be a premonitory sign of impending brain herniation and death, and its identification warrants immediate therapeutic intervention. In response to a progressive and near terminal decrease in cerebral perfusion as a result of intracranial hypertension, the brain triggers a massive sympathoadrenal-mediated release of catecholamines in a final attempt at preserving CPP. This response has evolved to increase the mean arterial BP and promote blood flow to the ischaemic brain. However, the catecholamine surge of the cerebral ischaemic response can cause several deleterious pathophysiological consequences, including:

- Severe systemic arterial hypertension that can result in end-organ damage (retinal detachments/haemorrhage) and reflexive bradycardia that occurs following the detection of systemic hypertension induced by vascular baroreceptors (the Cushing reflex).
- Non-cardiogenic pulmonary oedema.
- Brain–heart syndrome. Clinically, this will present as a variety of cardiac arrhythmias, resulting from myocardial ischaemia, that can have negative cardiovascular consequences.

In addition to neurological dysfunction, animals with an SBT may present for respiratory distress referable to the upper respiratory system in the case of neuroinvasive primary intranasal neoplasms (**374**), the lower respiratory system in the presence of pulmonary metastases, cardiovascular collapse from haemoabdomen or cardiac tamponade, or other problems related to the presence of a tumour in extraneural organs. Cases with pituitary apoplexy may present with non-specific signs of lethargy, gastrointestinal distress or collapse secondary to a hypoadrenocortical crisis.

In the absence of an identifiable cerebral ischaemic response, clinical detection of the terminal effects of intracranial hypertension, such as brain herniation, can be difficult. In animals with altered levels of consciousness, the detection of depressed CN functions, or changes in body posture (see Chapter 20), provides the most sensitive indication of impending or current brain herniation. However, CN dysfunction is not often present in the presence of brain herniation. A recent study found that only 1/28 dogs with isolated caudal transtentorial herniation seen on MRI had associated CN dysfunction. Forty percent of dogs with both caudal transtentorial and foramen magnum herniation had CN dysfunction on evaluation. A diminished or absent oculovestibular reflex, the development of unilateral or bilateral mydriasis and loss of the PLRs are suggestive of transtentorial brain herniation. Nystagmus, head tilt, gag reflex deficits and tongue weakness are suggestive of a foramen magnum herniation.

Although numerous pathological respiratory alterations (e.g. Cheyne–Stokes respiration, ataxic respirations, central mesencephalic hyperventilation) have been described in association with injuries to brainstem ventilatory centres as a result of brain herniations, their clinical characterization can be difficult and they should not be relied on for localization of injury or considered indicative of brain herniation.

DIFFERENTIAL DIAGNOSIS

Head trauma, cerebrovascular accident, infectious or non-infectious meningoencephalitis/granuloma, toxic or metabolic encephalopathy.

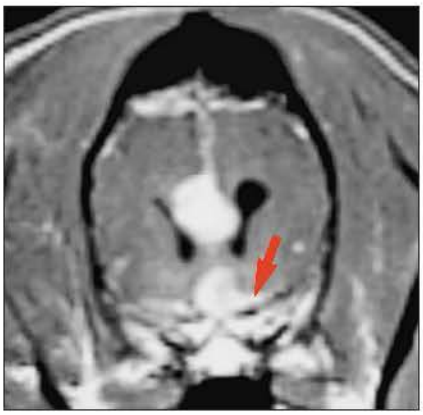
Table 91 **Neurological features of common veterinary intracranial neoplasms**

NEOPLASM TYPE	ANATOMICAL FEATURES	CT FEATURES	MRI FEATURES	PATTERN OF CONTRAST ENHANCEMENT	COMMENTS
Gliomas: oligodendroglioma, astrocytoma, mixed glioma	Solitary, intra-axial mass; well to poorly marginated; ovoid to amorphous; infiltrates parenchyma	Hypo- to hyperattenuating mass (**366**)	T1-weighted: hypo- to isointense; T2-weighted: isointense to hyperintense; FLAIR: hyperintense (**363**)	Variable and often heterogeneous; 'ring-enhancing' (**366**)	Oligodendroglioma has predilection for frontal lobes, more uniform shape and contrast or ring enhancing
Meningiomas	Solitary, extra-axial mass; broad based; well circumscribed; dural tail sign; calvarial hyperostosis; compresses parenchyma	Iso- to hyperattenuating mass; can be cystic/ hypoattenuating	T1-weighted: isointense or hypointense/cystic; T2-weighted: isointense to hyperintense; FLAIR: hyperintense (**375, 381**)	Usually marked, uniformly contrast enhancing (**360, 381a**); occasionally ring enhancing	Occasionally multifocal masses, especially in cats (**375**)
Choroid plexus tumours	Intraventricular or cerebellopontomedullary angle, extra-axial mass; secondary, obstructive hydrocephalus; spherical or lobular appearance	Hyperattenuating mass (**364**)	T1-weighted: hypo-, iso- or hyperintense; T2-weighted: iso- to hyperintense	Moderate to marked, uniform to heterogeneous enhancement (**362**)	Occasionally multifocal masses from drop metastases with carcinomas (**373**)
Pituitary neoplasms	Pituitary fossa/sella region, extra-axial mass; may displace suprasellar structures	Enlarged pituitary gland (**370**)	T1-weighted: isointense; T2-weighted: isointense to mixed iso- to hyperintense	Normal pituitary enhances; benign tumours have uniform enhancement (**369**)	Irregular shape or heterogeneous enhancement may indicate carcinoma; dynamic pituitary imaging can enhance detection of microtumours

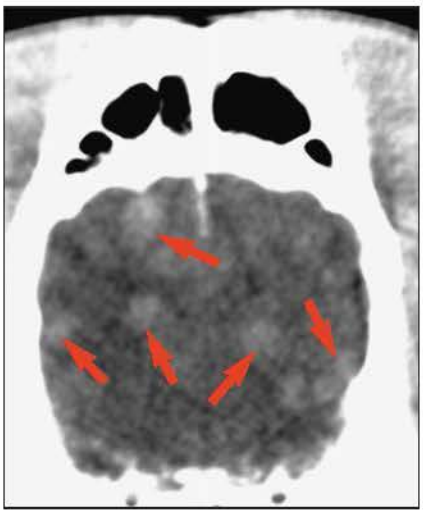
DIAGNOSIS

Definitive diagnosis of intracranial neoplasms is only possible following biopsy of representative neoplastic tissue. However, contemporary, presumptive antemortem diagnosis of intracranial neoplasia has been revolutionized by the superior anatomical detail and spatial resolution afforded by MRI techniques.

Advanced neuroimaging (CT or MRI) of the brain is the necessary first step in the antemortem diagnosis of intracranial neoplasia. Although diagnostic confirmation of a tumour can only be achieved after histopathological examination (tumour biopsy), specific neuroimaging features have been reported to correlate well with certain tumour types (*Table 91*). The majority of PBTs are associated with imaging evidence of a solitary mass lesion



▲ 375 Transverse post-contrast T1-weighted image from a dog with multifocal intracranial meningiomas in falcine and parasellar locations. A dural tail sign is evident in the parasellar location (arrow).



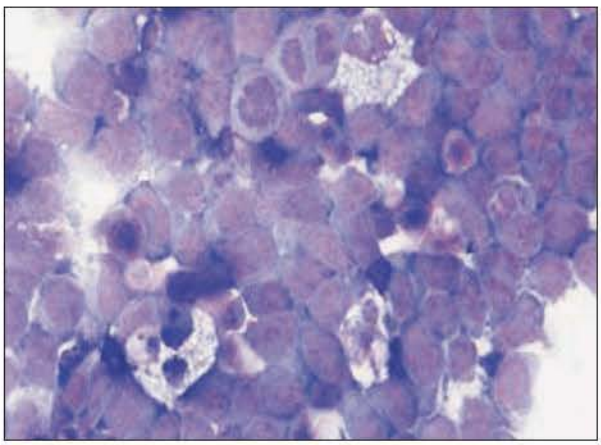
▲ 376 Transverse CT scan revealing multiple, variably hyperattenuating nodular lesions (arrows) throughout both cerebral hemispheres from a dog with metastatic splenic haemangiosarcoma.

▶ 377 CSF cytology demonstrating a homogeneous population of round cells compatible with lymphoma.

within the brain, although both meningiomas (**375**) and choroid plexus tumours (**362**) may be multifocal. The diagnostic imaging characteristics of SBTs are more heterogeneous, and depend on their tissue of origin as well as on the manner in which they involve the brain (i.e. local extension [**374a**] or distant haematogenous metastasis). Haematogenous brain metastases present as multifocal ovoid to spherical lesions in the cerebral watershed zone (i.e. the anatomical border between the grey and white matter [**376**]). Advanced neuroimaging may also offer additional information regarding the types of secondary tumour-associated pathological effects contributing to the clinical deterioration of the patient, such as brain oedema, obstructive hydrocephalus, haemorrhage, infarction or brain herniation, that are helpful to guide therapeutic decision making.

Computed tomography

Although less ideal for visualization of the neural parenchyma than MRI, newer-generation CT scanners are capable of imaging the calvarium in seconds, thus offering the advantage of superior image-acquisition speed and obviating the requirement for general anaesthesia in patients who are in a critical clinical condition. The use of CT imaging is common for the planning of radiotherapeutic treatments in animals with intracranial neoplasms. The CT features of common intracranial neoplasms are provided in *Table 91*.



Magnetic resonance imaging

MRI provides excellent detail with respect to the size, margination, tissue properties and neuroanatomical location of the tumour, as well as identification and differentiation of any concurrent secondary pathophysiological effects caused by the tumour. MRI is the preferred technique for the non-invasive antemortem diagnosis of intracranial neoplasms, as well as for surgical treatment planning. The MRI features of common intracranial neoplasms are provided in *Table 91*.

Cerebrospinal fluid collection

In animals with intracranial neoplasia, analysis of CSF commonly reveals non-specific abnormalities, particularly an elevated TP concentration. Exfoliation of neoplastic cells into CSF is uncommon and is typically associated with CNS lymphomas and choroid plexus carcinomas (**377**). Considering the overall low specificity of CSF analysis for the diagnosis of intracranial neoplasia and the potential risks (rapid decrease in ICP resulting in brain herniation), CSF collection is best performed after advanced neuroimaging procedures. This approach allows the clinician to best assess the comparative risks and benefits of the procedure in each individual patient.

Cytological and histopathological examination of brain tumour tissue

A definitive diagnosis of intracranial neoplasia may only be obtained via microscopic evaluation of tumour tissue. Histopathological examination of tissue samples is the most accurate and sensitive method, although intraoperative cytological preparations are also useful. Brain tumour biopsy samples are most often procured during therapeutic craniotomy procedures, but brain biopsy procedures can be safely performed using open free-hand surgical techniques, with minimally invasive stereotactic CT guidance or with ultrasound assistance. Definitive classification and grading of PBTs can be difficult in cases where the tumour is poorly differentiated.

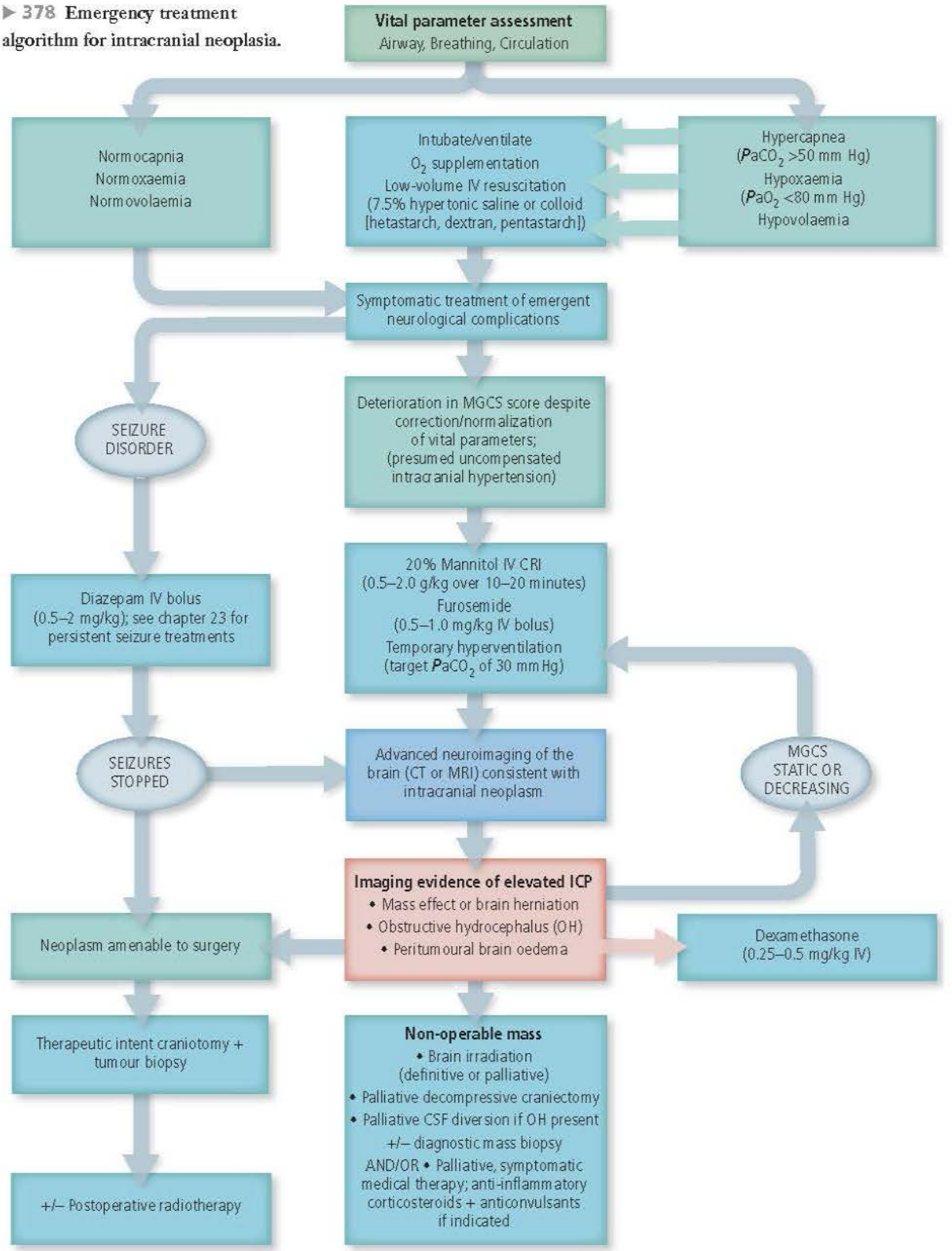
Systemic screening for extraneural disease

Intracranial neoplasms often affect middle-aged to geriatric animals, so routine haematology, serum biochemical profiles and urinalysis are helpful for the identification of significant concurrent systemic disease or secondary pathophysiological effects of the underlying brain tumour. Thoracic radiography, echocardiography and abdominal imaging (ultrasonography) are all indicated in animals with clinical complaints referable to organs in those body cavities, but should be considered in all patients, especially prior to performance of therapeutic cytoreductive surgery or brain irradiation. Retrospective studies have shown that concurrent, unrelated neoplasms are commonly identified in geriatric dogs with PBTs, and extraneural tumour foci are frequently present in the lung, heart and kidneys of dogs with SBTs. Intracranial meningiomas have also been occasionally reported to metastasize to the lung.

Electrophysiology

Electroencephalography and BAER are electrophysiological techniques that have been used in animals with intracranial neoplasms. The information that they provide is complementary to the history, clinical, neurological and neuroimaging examinations. Although these techniques are sensitive for the detection and occasionally for the neurolocalization of pathological processes within the brain, the identification of any abnormality is non-specific for the underlying aetiology.

▶ 378 **Emergency treatment algorithm for intracranial neoplasia.**



MANAGEMENT

Assessment and stabilization of systemic vital parameters are the first priorities. A patent airway and normal ventilation, normovolaemia,and normotension should be the initial treatment goals to optimize cerebral oxygenation and CPP. Secondary goals include intervening for emergent neurological complications, which include tumour-related seizure disorders, clinical neurological deterioration secondary to uncompensated intracranial hypertension and paraneoplastic metabolic derangements. For animals with paraneoplastic metabolic derangements, such as those seen with pituitary apoplexy and subsequent secondary hypoadrenocortical crisis or hypertonic dehydration with CDI, parenteral fluid therapy and medications should be administered as indicated (see Chapter 31). Once the patient is systemically stabilized, advanced neuroimaging studies are performed to prioritize the differential diagnoses and identify the appropriate ancillary diagnostic and therapeutic plans. A treatment algorithm is provided in **378**.

Treatment of secondary pathophysiological alterations

Seizures

The first-choice anticonvulsant in emergency situations is diazepam (0.5–2.0 mg/kg IV). If prompt intravenous access cannot be established, 1–2 mg/kg diazepam can be given per rectum. CRI of diazepam or propofol and intravenous loading doses of barbiturates may be considered for recurrent seizures or SE. (See Chapter 23 for additional specific treatment recommendations regarding recurrent seizures or SE.) Patients with secondary epilepsy due to intracranial neoplasm should be started on oral maintenance anticonvulsant drugs. If undesirable alterations in the patient's behaviour or interactions with the owner are present as a result of the tumour, the authors recommend the use of anticonvulsants that have less potential to further exacerbate sedation, such as levetiracetam (20 mg/kg PO or IV q8h) or felbamate (15 mg/kg PO q8h) in lieu of more traditional anticonvulsants (i.e. phenobarbital or bromide).

Brain oedema

Patients with evidence of mass effect (midline shift, attenuation of ventricles, brain herniation, oedema) can benefit from pharmacological therapies. Osmotic and loop diuretics are the mainstays of therapy for cerebral oedema in the acute period. Vasogenic oedema is the primary form of oedema treatable with diuretics.

Mannitol

Mannitol may be given intravenously (0.5–2.0 g/kg) as a slow bolus infusion, every 4–6 hours as needed. It is an osmotic diuretic that decreases ICP by drawing water out of the interstitial space; it is also a positive rheologic agent, decreasing the viscosity of blood and improving microvascular perfusion and CPP. It is recommended that mannitol is given as a slow bolus over 10–20 minutes, as a rapid bolus may increase intravascular volume before renal clearance, resulting in transiently but markedly increased ICP. Mannitol crystallizes at room temperature and should be kept warm prior to administration through a filter to prevent injection of crystals.

Furosemide

Furosemide (0.5–1.0 mg/kg IV) is given in conjunction with mannitol, typically during the last 5 minutes of the mannitol CRI. Furosemide is a loop diuretic that does not require an intact blood–brain barrier to be effective. Furosemide therapy is synergistic with mannitol in patients with elevated ICP in that it decreases CSF production, prolongs the osmotic effect of mannitol and can mitigate the transient rebound increment in ICP that may occur following mannitol administration.

Corticosteroids

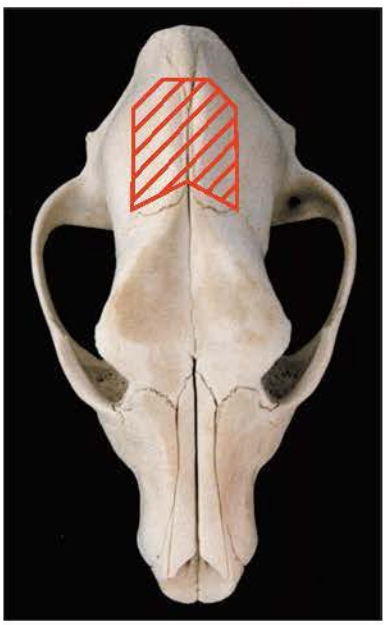
Corticosteroids (dexamethasone, methylprednisolone, prednisone) are effective at reducing peritumoural brain oedema and can be used in the acute emergency situation and continued chronically as a palliative treatment. The initially prescribed dose should approximate an anti-inflammatory dose (equivalent to 0.5 mg/kg of prednisone q12h), and can be titrated as necessary based on the individual patient's response. Individual patient responses to corticosteroids can be highly variable. In some instances, vasogenic oedema may be completely refractory to steroid therapy. The lowest possible dose of steroid that mitigates clinical signs should be used for chronic outpatient therapy.

Uncompensated intracranial hypertension

Hyperventilation

Many of these patients have loss of the normal pressure and chemical vascular autoregulatory mechanisms in addition to some degree of respiratory depression due to brainstem compression, resulting in hypercapnea and hypoxaemia. Hypercapnea stimulates cerebral vasodilation, which contributes to the increase in ICP by increasing cerebral blood volume. Transient hyperventilation to maintain a target $PaCO_2$ of 30 mmHg ($PETCO_2$ ~ 25 mmHg) can be considered to maximize CPP and maintain optimal cerebral blood volume in patients that have not responded to diuretic administration. However, since chemical autoregulatory mechanisms are often disrupted, the theoretical vasoconstrictive benefits of hyperventilation are probably non-uniform within the brain and so are associated with some degree of risk. Furthermore, excessive or chronic hyperventilation can be accompanied by a reduction in global CBF, which may drop below ischaemic thresholds. Therefore, it is not a recommended therapy unless the $PaCO_2$ can be closely monitored with capnography or arterial blood gas analysis (see Chapter 20).

▼ **379** Schematic representation of the intended calvarial defect (hatched area) when performing a bilateral rostrotentorial craniectomy.



Palliative, decompressive craniectomy

Removal of the skull with subsequent durotomy is a very effective procedure for reducing ICP. Decompressive craniectomies are usually performed following intracranial imaging to optimize the surgical approach, and can be combined with therapeutic intent cytoreductive surgery or diagnostic brain biopsy procedures. However, palliative craniectomy can also be performed with the sole intent of lowering life-threatening intracranial hypertension, particularly in cases where neoplasms are inoperable and future brain irradiation is being considered. In the absence of diagnostic information provided by advanced neuroimaging, the approach used for decompressive craniectomy is dictated by lateralizing deficits identified during the neurological examination. In the absence of localizing clinical signs, bilateral rostrotentorial craniectomy can be considered (**379**).

CSF diversion (ventriculoperitoneal shunting)

Diversion of CSF can be an effective procedure for reducing ICP. This technique can be performed via ventriculostomy or ventriculoperitoneal shunting. Ventriculostomy involves insertion of a catheter into the ventricular system of the brain for the purposes of withdrawing CSF and/or implantation of an ICP monitoring device. Ventriculostomy is often performed in humans with a minimally invasive burr-hole craniectomy technique, as anatomical landmarks for catheter placement are well described. In veterinary patients, however, patient size and skull conformational differences, as well as pathological shifts in anatomical structures due to intracranial mass effect, often hamper performance of minimally invasive ventriculostomy. Ventriculoperitoneal shunting is occasionally indicated as an adjunctive therapeutic procedure in animals with obstructive hydrocephalus, particularly in cases where the neoplasm causing the obstruction is inoperable, and the patient requires stabilization in preparation for other primary therapy (radiation). Diversion of CSF from the ventricular system to the peritoneal cavity is efficacious at improving clinical signs associated with intracranial hypertension. Shunt-related complications (overshunting/slit-ventricle syndrome, obstruction, dislodgement) can occur and generally require surgical shunt revision.

Specific treatment of intracranial neoplasia

Cytoreductive craniotomy/craniectomy

The surgical approach employed in individual cases is primarily dictated by the neuroanatomical location of the neoplasm, which is identified with advanced neuroimaging. In general, superficially located, rostrotentorial and extra-axial tumours are the most amenable to surgical removal. Intra-axial and caudotentorial neoplasms are inherently more technically demanding, but can be surgically treated in some instances, especially when involving the superficial aspects of the cerebellum. Although somewhat intuitive, in the case of low-grade intracranial neoplasms (e.g. many meningiomas), recent literature suggests that the success of surgery appears to be related to the completeness of the surgical excision. Devices that assist with gross total tumour removal by improving intraoperative visualization (e.g. intracranial endoscopy) or techniques that facilitate removal of microscopic disease at the tumour margin (e.g. ultrasonic surgical aspirators or cortical resection) have been associated with prolonged survival (2–3 years) in dogs with meningiomas treated surgically.

Radiotherapy

Multiple types of brain irradiation have been used to treat brain tumours in dogs and cats including orthovoltage, cobalt-60, megavoltage external beam radiotherapies and interstitial brachytherapies. Irradiation of intracranial tumours has been shown to be effective at improvement of tumour-associated neurological dysfunction and prolongation of survival, especially when compared with palliative medical therapy. The current standard of care is delivery of external beam radiotherapy using fractionated dose prescriptions, but hypofractionated therapies and single session, stereotactically-delivered radiotherapy using conventional linear accelerators or dedicated stereotactic radiosurgical systems (GammaKnife™, [**380**]; CyberKnife®) are currently being used and investigated at a few veterinary centres. Tumour-specific treatment planning techniques and dose prescriptions can vary considerably among veterinary radiation oncologists. Palliative radiation alone can have a significant and rapid beneficial effect on neurological status in some cases.



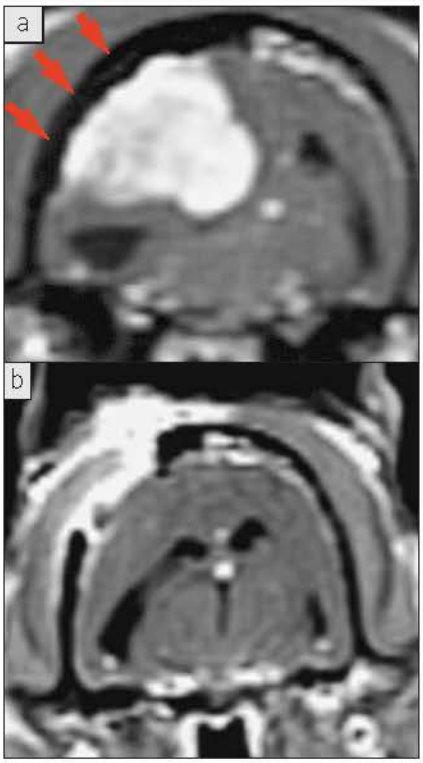
▲ **380** **Patient being positioned in the CT scanner for GammaKnife ™ stereotactic radiosurgical treatment planning using a custom-modified Leksell headframe.**

Cytotoxic chemotherapy

To date, there have been no objective, data-based studies investigating or demonstrating in-vivo efficacy for any systemically administered chemotherapeutic drug for the treatment of veterinary intracranial tumours. Currently, chemotherapy should be considered an empirical adjunctive therapy for intracranial neoplasms. Therapeutic obstacles that may hamper the efficacy of systemic chemotherapy include large tumour burdens at diagnosis and problems with effective delivery across the blood–brain barrier. Rare case reports have shown some measurable therapeutic responses of intracranial tumours to nitrosourea drugs such as lomustine (60–90 mg/m^2 PO every 3 weeks in dogs; 50–60 mg/m^2 PO every 3 weeks in cats) and carmustine (50 mg/m^2 IV every 6 weeks in dogs) that will cross the blood–brain barrier. Hydroxyurea (50 mg/kg/day PO in dogs, 10 mg/kg/day PO in cats) has been shown to be cytotoxic to human meningioma cell lines in vitro, and has been used as an adjunctive treatment for canine meningiomas. These compounds are therefore prescribed by some clinicians to treat intracranial neoplasms. CNS lymphoma may respond to combination chemotherapy with multiagent protocols that include cytosine arabinoside.

Obstacles to drug delivery have been mediated in humans with brain tumours through topical infusion of chemotherapeutics in tumour resection cavities via implantable catheters, convection-enhanced drug delivery strategies or interstitial implantation of chemotherapeutic impregnated wafers within the brain.

▼ **381** (a) Preoperative, transverse post-contrast T1-weighted MR image from a 12-year-old cat with circling and seizures. An extra-axial, markedly enhancing mass is present in the right parieto-occipital lobes of the cerebrum, resulting in compression of the right lateral ventricle. Hyperostosis of the calvarium can be seen (arrows). (b) Transverse, post-contrast T1-weighted image taken 2 years following craniectomy. The cat was clinically normal with no evidence of tumour recurrence. The craniectomy defect in the calvarium is apparent.



PROGNOSIS

The prognosis for patients with PBTs and SBTs is dependent on numerous factors such as tumour type and grade, neuroanatomical tumour location, severity of neurological deficits and type of treatment(s) administered. Symptomatic medical therapies, such as prednisone and anticonvulsants, have had survival times of 6–56 days reported in dogs with brain tumours, although survivals of > 6 months are possible in some mildly affected animals with forebrain tumours treated palliatively. Multiple studies have reported that the severity of neurological dysfunction is negatively correlated with survival in animals treated for intracranial neoplasms. Additionally, animals with rostrotentorial tumours survive longer than those with neoplasms in caudal tentorial locations if treated with similar techniques.

In cats with meningiomas, median survivals of >2 years have been reported following successful cytoreductive surgery (**381**), with presumed or confirmed tumour recurrences documented in about 20% of operated cats.

There is also evidence in the literature that survival of dogs with intracranial meningiomas is superior (median survival, 16 months) when multimodal treatment, consisting of cytoreductive surgery and postoperative external beam radiotherapy, is administered when compared with surgical treatment alone (median survival, 7 months). Irradiation of intracranial masses has been shown to be safe and associated with tolerable adverse effects, and efficacious at improving clinical signs of brain dysfunction and prolonging survival in animals in which surgical resection was not possible or performed. However, extrapolation of tumour-specific, evidence-based prognostic information from these radiotherapeutic studies is hampered by the fact that histopathological confirmation of the mass as an intracranial neoplasm was not a universal inclusion criterion.

Transsphenoidal hypophysectomy and pituitary irradiation have also been shown to be safe and efficacious treatments for functional pituitary adenomas in dogs and cats. Studies investigating the efficacy of various treatments and outcomes in dogs and cats with histologically confirmed PBTs of neuroectodermal origin or metastatic SBTs are sufficiently rare to preclude provision of any evidence-based prognostic information about these types of tumours.

METABOLIC ENCEPHALOPATHIES

Kate Chandler & Robert Goggs

INTRODUCTION

Metabolic encephalopathy is a clinical syndrome resulting from disorders of metabolism. It is characterized by altered mental state and neurological deficits due to disruption of brain function and structure secondary to energy deprivation, derangements of electrolytes, acid–base balance or accumulation of endogenous toxins. Metabolic encephalopathy is not a single entity, but a heterogeneous and frequently multifactorial condition. It is commonly encountered in the critical care setting and arises secondary to conditions such as liver dysfunction, endocrinopathy or renal failure. Endogenous metabolic diseases due to inborn errors of CNS metabolism also occur occasionally.

Metabolic encephalopathies typically cause diffuse, symmetrical forebrain signs. Onset may be acute or chronic and signs may wax and wane. The earliest and most consistent signs are depression of consciousness and generalized seizures. Other neurological signs vary with the type and severity of the metabolic disturbance.

Common historic signs associated with metabolic encephalopathy include:

- Waxing and waning neurological signs/behaviour change.
- Temporal relationship between feeding and neurological signs.
- Seizure activity.
- Altered mentation.
- Blindness.
- Gastrointestinal signs.
- Increased or decreased appetite.
- Pica.
- Dermatological signs (e.g. alopecia).
- Tremor.

Common clinical signs of metabolic encephalopathies include:

- Predominant forebrain signs (and/or brainstem):
  - Seizures.
  - Behaviour change: aggression, anxiety, dementia, mania.
  - Obtundation/stupor/coma.
  - Blindness with normal PLRs (amaurosis).
- Symmetrical neurological deficits.

The key to successful treatment in these patients is (1) rapid identification of underlying causes; (2) rapid treatment of metabolic abnormalities; (3) effective monitoring to rapidly identify potentially life-threatening abnormalities. Effective symptomatic treatment is frequently the difference between success and failure.

ELECTROLYTE DISTURBANCES

Sodium disorders

Most disorders of sodium concentration result from disorders of water balance. Both hyper- and hyponatraemia can cause neurological dysfunction via alterations in neuronal cell volume and function. Slow, gradual alterations in sodium concentration are well tolerated until concentrations become extreme. Small absolute changes that occur rapidly may cause more profound neurological dysfunction than larger more gradual alterations.

Hypernatraemia

Overview

Blood sodium levels reflect the ratio of sodium to water in the extracellular fluid and account for most of the osmotically active particles in serum. Hypernatraemia is indicative of an increase in total body sodium relative to total body water. It occurs secondary to net solute gain, sodium-free water loss or hypotonic fluid loss.

Aetiology/pathophysiology

Causes of hypernatraemia include:

- Net solute gain: excess salt intake associated with salt poisoning, administration of intravenous hypertonic saline or sodium bicarbonate. Water loss and salt gain can also occur with hyperaldosteronism and hyperadrenocorticism.
- Sodium-free water loss: diabetes insipidus, primary hypodypsia, water unavailable or patient unable to drink, heat stroke.
- Hypotonic fluid loss: gastrointestinal loss (vomiting, diarrhoea, small intestinal obstruction), third space loss (pancreatitis, peritonitis), osmotic diuresis (mannitol infusion, hyperglycaemia), chemical diuresis (furosemide), non-oliguric renal failure, chronic renal failure, postobstructive diuresis.

Hypernatraemia can be further divided into hypovolaemic (hypotonic loss), normovolaemic (sodium-free water loss) and hypervolaemic (net solute gain) forms. Hypernatraemia due to a gain of sodium results in increased extracellular fluid (ECF) (hypervolaemic hypernatraemia). Pure water loss results in relative preservation of ECF due to equilibration with ICF (normovolaemic hypernatraemia), while hypotonic fluid loss results in decreased ECF volume (hypovolaemic hypernatraemia). With the latter, affected patients are therefore more likely to show signs of volume depletion (tachycardia, increased capillary refill time, weak pulse). Evaluation of the volume status of the patient is therefore important in the process of identifying the underlying cause of hypernatraemia and the treatment approach.

The increase in serum sodium creates a hypertonic state in the ECF. Hypernatraemia leads to cell shrinkage secondary to osmotic water movement into the hyperosmolar interstitium. The decrease in brain volume caused by cellular dehydration can cause tearing of small intracranial blood vessels and haemorrhage (subarachnoid, subdural and/or intraparenchymal).

Clinical presentation

The cells of the CNS are very intolerant of the volume changes described above and this leads to clinical signs including obtundation, head pressing, seizures, ataxia, tremors, blindness and coma. In addition, signs of volume depletion are often present in hypernatraemia secondary to hypotonic fluid losses, while signs of hypervolaemia (e.g. pulmonary oedema) may be present in cases of net solute gain. Clinical signs typically develop if the sodium concentration alters at a rate of >1 mmol/l/hour (>1 mEq/l/hour) or if the absolute sodium concentration exceeds 180 mmol/l (180 mEq/l). If sodium concentrations alter slowly, the brain adapts by producing idiogenic osmoles such as taurine, sorbitol and inositol. These molecules increase intracellular osmolality, buffering cell volume against the increased extracellular sodium concentration. Rapid correction of chronic hypernatraemia (>0.5–1 mmol/l/hour [>0.5–1 mEq/l/hour]) can lead to osmotic gradient reversal, inducing water to move into cells and causing cell swelling, cerebral oedema and clinical signs of intracranial hypertension.

Management

Treatment of hypernatraemia

The underlying cause and sodium abnormality should be identified and treated. There is no standard method of correction to suit all situations, therefore treatment should be individualized, aiming to replace the water deficit and treat the underlying cause. Correction of sodium concentration should occur at the same rate at which it developed (i.e. rapid in cases of salt intoxication; slowly in cases of fluid loss). The rate of blood sodium change should not exceed 0.5–1 mmol/l/hour (0.5–1 mEq/l/hour). If serum sodium concentrations are lowered too quickly, cerebral oedema may result, with a clinical deterioration in consciousness. Blood sodium concentration should be monitored every 4–6 hours during correction.

Treating hypernatraemia secondary to fluid loss

A hypovolaemic, hypernatraemic patient should be volume resuscitated with a fluid containing a sodium concentration equal to that of the patient. This can be created by adding aliquots of a concentrated NaCl solution such as 7.2% saline (1.23 mmol [mEq] NaCl per ml) to an isotonic replacement crystalloid solution such as 0.9% saline or Hartmann's solution. For example, a patient with a plasma sodium concentration of 181 mmol/l (181 mEq/l) will need a solution that contains 181 mmol/l (181 mEq/l) NaCl (equivalent to a 1.06% solution). This can be prepared by increasing the sodium concentration of 0.9% saline (154 mmol/l [154 mEq/l]) by adding 27 mmol (27 mEq) of NaCl per litre. This is achieved by adding 22 ml of 7.2% saline to 1,000 ml of 0.9% saline. (*Note:* 1,000 ml fluid bags typically contain an excess of 20 ml, which will need to be removed prior to addition of the 7.2% saline.) The sodium concentration of the resultant solution should be checked using an electrolyte analyser prior to bolus administration to the patient.

Following volume resuscitation, the hypernatraemic patient's free water deficit should be replaced slowly to reduce sodium concentration at a rate of 0.5–1.0 mmol/l/hour (0.5–1.0 mEq/l/hour). If a recent body weight is available, the following equation can be used to approximate the free water deficit:

$$\text{Free water deficit (l)} = 0.6 \times \text{body weight (kg)} \times ([\text{measured } Na^+/\text{normal } Na^+] - 1)$$

The predicted change in blood sodium concentration from administration of one litre of fluid can be calculated using the following equation:

$$\text{Change in } Na^+ = \frac{\text{infusate } Na^+ - \text{blood } Na^+}{(\text{body weight (kg)} \times 0.6) + 1}$$

Free water replacement can be achieved with a range of fluids. If significant ongoing losses such as diarrhoea are occurring, the use of 0.9% saline or Hartmann's solution will be safer. Hypotonic fluids, such as 0.45% saline or 5% dextrose in water, can be used if ongoing losses are minimal. Hypotonic fluids will reduce the sodium concentration more rapidly than an equal volume of isotonic fluid (see Chapter 31 for further details).

Treating hypernatraemia secondary to sodium gain

With hypernatraemia, patients are typically hypervolaemic, may have elevated systemic BP and are at risk of pulmonary oedema. Furosemide (1–2 mg/kg IV) will facilitate loss of both sodium and excess fluid. Five percent dextrose in water can be used to correct the sodium concentration. Should the sodium concentration drop more rapidly than >0.5 mmol/l/hour (>0.5 mEq/l/hour), this may need to be altered to 0.45% saline or Hartmann's solution. Frequent monitoring of blood sodium concentrations will guide the use of furosemide and fluid therapy.

Hyponatraemia

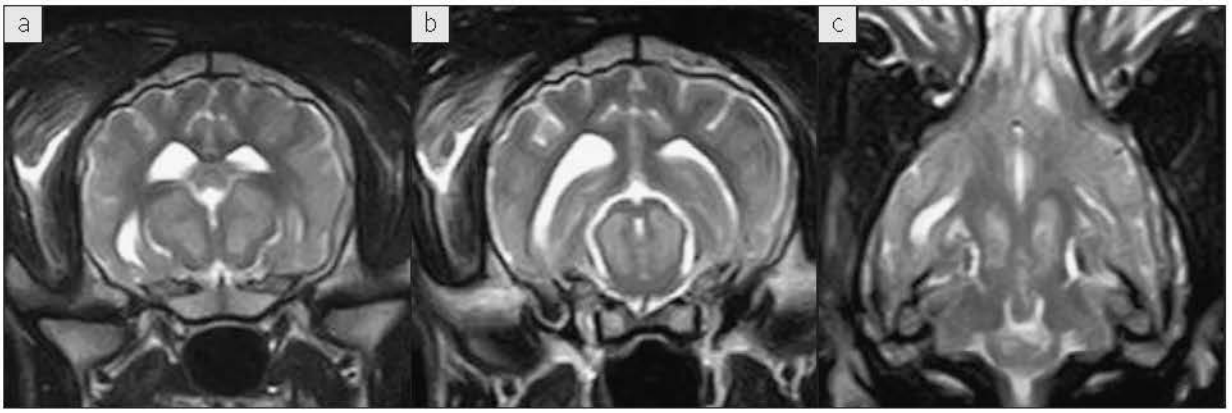
Overview

Hyponatraemia occurs primarily due to loss of salt, gain of water, gain of hypotonic fluid or addition of hypertonic solution without sodium (glucose or mannitol).

Apart from hyperglycaemia and mannitol administration, which may lead to hyponatraemia and hyperosmolality, most hyponatraemic patients are hypo-osmolar. Hyponatraemia with low plasma osmolality may be accompanied by normal plasma volume (syndrome of inappropriate antidiuretic hormone secretion [SIADH], psychogenic polydypsia, hypotonic fluid infusion), decreased plasma volume (Addison's disease, gastrointestinal and third space loss) or increased plasma volume (congestive heart failure, severe liver disease, nephrotic syndrome, advanced renal failure). As for hypernatraemia, determination of the volume status of the patient is essential in the process of identifying the underlying cause of the hyponatraemia and the treatment approach.

Aetiology/pathophysiology

Hyponatraemia leads to cell swelling and cerebral oedema secondary to osmotic water movement into cells. A gradual change in sodium concentration allows cells to adapt by expelling intracellular solutes to decrease intracellular osmolality and restore normal cell volume. Rapid correction (>0.5–1.0 mmol/l/hour [>0.5–1.0 mEq/l/hour]) of hyponatraemia can cause severe cell shrinkage as water moves into the increasing osmolality of the extracellular environment. This shrinkage can separate the neurons from their myelin covering, leading to myelinolysis. In humans this occurs predominantly in the pons (central pontine myelinolysis; also known as



▲ **382** Transverse (a, b) and dorsal (c) T2-weighted MR images of a Collie-cross dog with osmotic demyelination syndrome following rapid correction of hyponatraemia. Note the bilaterally symmetrical hyperintensities affecting the thalamic and mesencephalic grey matter.

osmotic demyelination syndrome), while in dogs it occurs principally in the thalamus (**382**).

Clinical presentation

Mild to moderate hyponatraemia is typically occult. Severe hyponatraemia, where sodium concentrations are less than 120 mmol/l (120 mEq/l) or rapid decreases in sodium concentration (>1 mmol/l/hour [>1 mEq/l/hour]) occur, are associated with obtundation, head pressing, seizures and coma. In addition, hyponatraemic patients may have signs of dehydration and hypovolaemia (e.g. rapid and weak pulse, hypotension, cold extremities, prolonged capillary refill time), while hypervolaemic patients may be presented with ascites, pulmonary oedema, peripheral oedema or jugular distension.

Management (see Chapter 31 for further details)

Both the underlying cause and the sodium abnormality should be identified and treated. Hyponatraemia almost always develops slowly; therefore, hyponatraemia must be corrected slowly to avoid life-threatening neurological damage (osmotic demyelination syndrome), which may take several days to become evident. Sodium concentrations should be monitored every 4–6 hours during correction. The hypovolaemia should be corrected using 0.9% saline. The rate of sodium correction should not be >0.5 mmol/l/hour (>0.5 mEq/l/hour). Hypertonic saline is rarely required for the treatment of hyponatraemia. An exception to these recommendations are patients with SIADH, who may require a combination of water restriction and a slow continuous infusion of hypertonic (3%) saline to normalize their sodium concentration. Specific criteria should be used to diagnose this uncommon condition, including measuring plasma sodium and plasma osmolality, measurement of urine osmolality or urine sodium, assessment of renal, adrenal and thyroid function, and evaluation for ascites or oedema. Further information on the diagnosis and treatment of SIADH can be found in Chapter 31.

Hypoperfused patients may be depressed and this should not be confused with the neurological signs of hyponatraemia (e.g. seizures, coma). Seizures due to sodium abnormalities should be treated with diazepam (0.5 mg/kg IV or per rectum).

Hypocalcaemia

Overview

Calcium homeostasis is based on a complex interplay of parathyroid hormone (PTH), calcitriol and calcitonin. Ionized calcium concentrations (iCa^{2+}) are usually tightly controlled. PTH is responsible for minute-to-minute changes and acts to increase iCa^{2+}. Calcitriol (1,25 dihydroxyvitamin D) is synthesized in the kidney under the influence of PTH. Calcitriol is responsible for day-to-day changes and also acts to increase iCa^{2+}. Calcitonin acts to reduce postprandial increases in iCa^{2+} (**383**).

Aetiology/pathophysiology

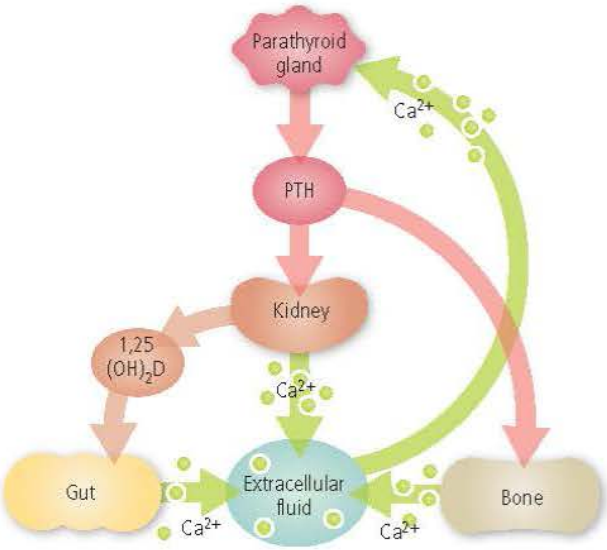
Hypocalcaemia may result from renal failure, eclampsia, pancreatitis, ethylene glycol intoxication or primary hypoparathyroidism. Iatrogenic hypocalcaemia occurs following thyroidectomy or parathyroidectomy, phosphate enema administration or citrate anticoagulant overdose following transfusion. Hypocalcaemia lowers the threshold for neuronal and muscle depolarization as a result of alterations in sodium flux and membrane potentials.

Clinical presentation

Clinical signs of hypocalcaemia include facial rubbing, muscle twitching, cramping, tetanic tremors, ataxia and seizures. Hypotension and tachyarrhythmias may also occur.

Diagnosis

Diagnosis is based on recognition of characteristic clinical signs and confirmation of ionized hypocalcaemia, which is typically <1.0 mmol/l (<4.0 mg/dl). A number of point-of-care technologies are available for rapid measurement of ionized calcium. Serum biochemistry profiles typically report total calcium, which is a poor indicator of ionized calcium concentrations (the biologically active fraction). Correction formulae exist, but their use is not recommended because their inaccuracy in predicting iCa^{2+} precludes safe treatment of hypocalcaemia. Primary hypoparathyroidism can be diagnosed by radioimmunoassay determination of plasma PTH concentration.



▲ **383** **Calcium physiology and the roles of parathyroid hormone (PTH) and calcitriol (1,25$(OH)_2D$) in calcium homeostasis. The principal action of PTH is to raise calcium levels in extracellular fluid (ECF) by increasing renal tubular resorption of calcium, mobilizing calcium from bone and increasing intestinal (gut) calcium absorption. Actions on bone and kidney are mediated directly through interaction with specific receptors. Action on gut is indirectly mediated by 1,25$(OH)_2D$, whose synthesis in the kidney is stimulated by PTH. Extracellular calcium feeds back to the parathyroid gland, inhibiting further secretion of the hormone.**
(Adapted from Habener JF, Rosenblatt M, Potts JT (1984) Parathyroid hormone: biochemical aspects of biosynthesis, secretion, action, and metabolism. *Physiol Rev* 64:985–1053.)

Management

Hypocalcaemia should be treated only if clinical signs are present. Calcium gluconate 10% (0.5–1.5 ml/kg [providing 5–15 mg/kg calcium] as a slow IV bolus over 10–30 minutes) can be administered. A continuous ECG should be monitored because of the risk of cardiotoxicity. There is significant risk of cardiac arrest during rapid administration. The infusion should be stopped immediately if bradycardia, increased P-R interval,

prolonged QRS complex, shortened QT interval on ECG or vomiting occurs. Subacute therapy for hypocalcaemia is provided with 10% calcium gluconate solution at a dosage of 5–10 ml/kg given slowly intravenously in lactated Ringer's solution or isotonic (0.9%) NaCl maintenance infusion over a 24-hour period. Serum calcium concentration must be monitored every 1–3 days and dosage adjustments made every 1–3 days based on serum levels to avoid iatrogenic hypercalcaemia. Long-term maintenance requires oral calcium (25 mg/kg q8–12h) and vitamin D supplementation.

ENCEPHALOPATHIES

Endocrine encephalopathy

Patients with endocrine encephalopathy may present with numerous clinical abnormalities such as electrolyte disturbances or seizures, requiring specific treatment or symptomatic therapy, respectively. The underlying disease must be identified and specific therapy initiated. Intravenous or rectal diazepam is an appropriate choice for seizures in these patients. A phenobarbital loading protocol is an appropriate second choice, providing hepatic function is normal (see Chapter 23).

Hypothyroid myxoedema coma

Overview

Myxoedema coma is an extreme life-threatening form of canine hypothyroidism.

Aetiology/pathophysiology

Myxoedema coma pathophysiology is incompletely understood. Doberman Pinschers seem to be overrepresented. Thyroid hormones indirectly regulate multiple cell functions affecting catabolism, metabolism and development. They also play permissive roles in multiple organ systems. The altered mental status in this condition results from direct effects of reduced thyroid hormone concentrations, and indirectly from decreased CBF, cerebral oedema and hyponatraemia. Myxoedema coma is typically precipitated by an event that overwhelms normal homeostasis such as infection or concurrent administration of thyroid hormone-altering medication or surgery, although in dogs no single event has been repeatedly identified.

Clinical presentation

Patients with this rare endocrine emergency may present with mental dullness, stupor or coma. In dogs, typical clinical signs include obesity, oedema, mental dullness, hypothermia, bradycardia, hypotension and hypoventilation. Stupor and coma are less common. CN dysfunction (especially facial and vestibular) can also be noted.

Diagnosis

Identification of profoundly low serum thyroxine levels (or free thyroxine levels by equilibrium dialysis) ± increased thyroid-stimulating hormone (endogenous TSH) levels assists with diagnosis. Interference from intercurrent disease must be considered when interpreting thyroid function tests in sick patients. Blood gases may reveal hypoxaemia and hypercarbia. Patients may be hypoglycaemic and have other biochemical changes consistent with hypothyroidism (e.g. hypercholesterolaemia, hyponatraemia). Electrocardiography may identify bradyarrhythmias, and response to treatment may actually aid in diagnosis. Investigation must also be directed towards identifying a predisposing cause such as infection, recent drug therapy or heart failure.

Management

The respiratory status must be assessed and oxygen and ventilatory support provided if required. Warmed intravenous fluid therapy ± supplementary glucose should be given as appropriate, together with passive external rewarming. L-thyroxine (1–5 g/kg IV q12h) should be given. Resolution of abnormal mentation, ambulation and systolic hypotension should be expected within 30 hours. Injectable levothyroxine may not be readily available, in which case oral levothyroxine may be administered via an orogastric tube. A liquid preparation is available and may be sourced from a local hospital. Care must be taken to avoid aspiration if the patient is obtunded or stuporous. Serum thyroxine levels should be monitored daily and oral levothyroxine begun once serum thyroxine levels are normal and appetite has resumed. This may take several days.

Prognosis

The prognosis is guarded and is poor if intercurrent disease is also present.

Thyrotoxicosis/thyroid storm

Overview

Hyperthyroidism or thyrotoxicosis describes the condition of excess thyroid hormone concentrations, while the term thyroid storm refers to a life-threatening multisystemic syndrome resulting from this condition.

Aetiology/pathophysiology

Thyroid storm syndrome consists of pyrexia combined with CNS, cardiovascular and gastrointestinal dysfunction. This syndrome occurs due to the combination of high basal thyroid hormone concentrations coupled with a rapid increase in hormone concentrations, sympathetic nervous system hyperactivity and increased cellular response to thyroid hormones. This condition may be precipitated by infection, surgery, non-thyroidal illnesses, aggressive thyroid palpation, iodine administration or abrupt cessation of antithyroid medication.

Clinical presentation

Hyperthyroid cats may present with restlessness, hyperactivity, anxiety, pacing, circling and occasionally focal or generalized seizures. Some cats may display a paradoxical apathy characterized by dullness and depression. Neurological signs include behavioural change, agitation, seizures and coma.

Diagnosis

A total thyroxine level above the reference interval is diagnostic if appropriate clinical signs are present, particularly if the history is consistent with a predisposing event. Hyperthyroidism with non-thyroidal illness may have thyroxine values within the normal reference range. The clinician should suspect this if a goitre is present.

Management

Treatment is directed at the provision of supportive therapy, the reduction of thyroid hormone production, the systemic effects of excess thyroid hormones and the identification and treatment of precipitating factors. Careful assessment of cardiopulmonary function is vital. Some patients may present in congestive heart failure and thus supportive therapies, such as oxygen therapy, and diuretic and vasodilator administration may be necessary. Judicious use of antiarrhythmics may be necessary. Atenolol (0.5–2.0 mg/kg PO q24h) or esmolol (0.1–0.5 mg/kg IV over 1 minute) may be required for treatment of supraventricular tachyarrhythmias, but care must be taken not to cause hypotension due to negative inotropy. Methimazole (2.5 mg/cat and 2.5–5.0 mg/dog PO q12h) is the drug of choice for thyroxine synthesis suppression. Investigation of an underlying precipitating process should be undertaken concurrently with initial stabilization.

Prognosis

The prognosis is guarded in the acute stages. The syndrome is poorly recognized, which may increase mortality. With appropriate management patients may be stabilized sufficiently to permit more definitive treatment (e.g. thyroidectomy or ^{131}I therapy).

Parathyroid disease

Overview

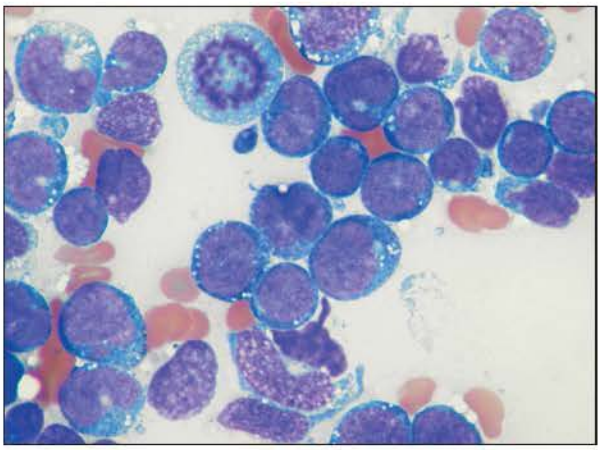
Primary hyperparathyroidism (PHPTH) results from excessive PTH secretion by neoplastic chief cells. The condition is characterized by high PTH concentrations, hypercalcaemia, hypophosphataemia and hyperphosphaturia.

Clinical presentation

Clinical signs include polyuria, polydipsia, vomiting, weakness, abdominal pain, constipation and anorexia. Approximately half of canine patients with PHPTH demonstrate listlessness, depression and lethargy. This is likely to be due to reduced CNS excitability secondary to the effects of hypercalcaemia on the neuronal membrane potential. In 10% of dogs, PHPTH causes muscle twitching and, more rarely, seizure activity secondary to hypercalcaemia, cerebral thromboembolic events or vasospasm. These events are more likely to occur in feline patients with ionized calcium concentrations >1.75 mmol/l (>7.0 mg/dl). In canine patients a hypercalcaemic crisis is likely in patients with ionized calcium concentrations >1.88 mmol/l (>7.5 mg/dl).

Differential diagnosis

In dogs the differentials include: lymphoma; anal sac apocrine gland adenocarcinoma; multiple myeloma; acute and chronic renal failure; hypoadrenocorticism; vitamin D intoxication (cholecalciferol or calcipotriene); granulomatous disease.



◀ **384** **Popliteal lymph node aspirate of a dog with ionized hypercalcaemia. Cytology reveals numerous large lymphoid cells with irregular nucleolated nuclei and minimal basophilic cytoplasm, and a single atypical mitotic figure, consistent with a large cell lymphoma.**

Idiopathic hypercalcaemia and neoplasia are the most common differentials in cats followed by renal failure (elevation of total calcium but usually not ionized calcium).

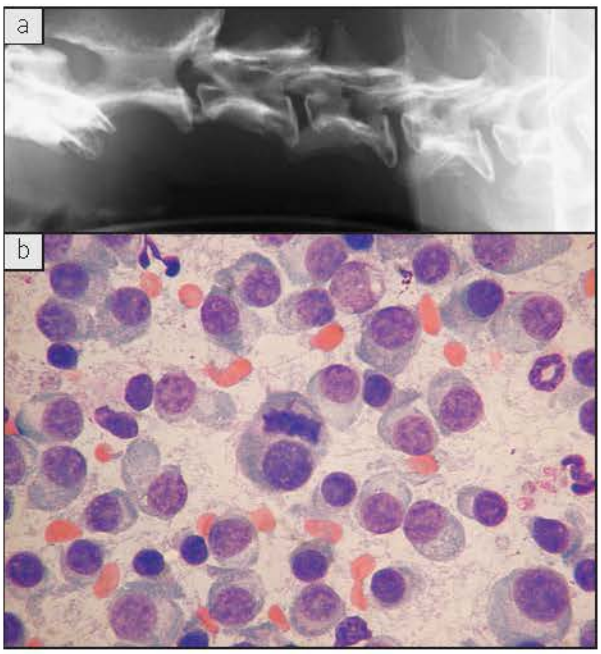
Diagnosis

The investigation of suspected PHPTH must focus on differentiating it from other causes of hypercalcaemia. Investigations include assays of total and ionized calcium, lymph node cytology (**384**), CBC, serum biochemistry, urinalysis, spinal (**385**) and abdominal imaging, splenic cytology (**385**), ACTH stimulation testing and assays of PTH and parathyroid hormone-related protein (PTHrP). Patients with PHPTH typically have total and ionized hypercalcaemia and inappropriately normal or increased PTH with normal PTHrP concentrations. Patients with only PHPTH will demonstrate an increase in serum cortisol concentrations following ACTH stimulation.

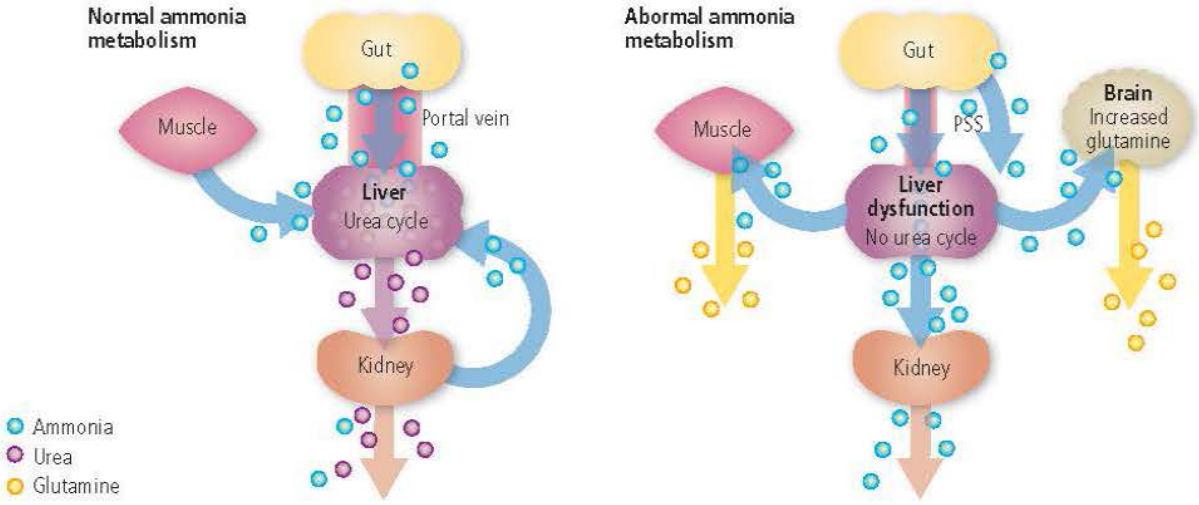
Management

Aggressive therapy will be required in patients with very high calcium levels. High Ca:Phos ratio (>5.6 SI units [>70 US units]) are unlikely in PHPTH, but are possible with other causes of hypercalcaemia. Treatment for PHPTH typically involves surgical resection of the parathyroid mass.

The most important therapeutic measure is to rehydrate the patient. Isotonic NaCl is the fluid of choice, as 0.9% NaCl competitively inhibits renal tubular absorption of calcium and urinary calcium excretion is enhanced by saline infusion. Therapy for hypercalcaemia consists of diuresis with 0.9% saline, furosemide (2 mg/kg IV q4–6h), calcitonin (4–6 IU/kg SC q8–12h) or bisphosphonates (e.g. pamidronate, 1.3–2.0 mg/kg in 0.9% saline as a CRI over 2 hours). The infusion rate of 0.9% saline should be rapid enough to produce intense diuresis, but care must be taken to avoid plasma overload. If possible, CVP measurements should be taken intermittently and the infusion slowed down or discontinued when the CVP



▲ **385** **(a) Lateral radiograph of the cervical spine and (b) splenic aspirate of a 8-year-old Doberman Pinscher presented with multifocal spinal pain, polyuria, polydipsia and lethargy. Serum biochemistry revealed elevated ionized hypercalcaemia and marked elevation in serum globulin. The radiograph reveals multiple osteolytic skeletal lesions scattered throughout the cervical vertebrae. The splenic aspirate shows numerous pleomorphic plasma cells alongside low numbers of small lymphocytes and rare neutrophils. The central plasma cell shows aberrant mitosis, consistent with (multiple) myeloma. (Photo courtesy Roger Powell)**



▲ **386** **Ammonia metabolism. In an animal with normal hepatic function, ammonia synthesized in the gut is transported to the liver via the hepatic portal vein. Approximately 90% of ammonia delivered to the liver is converted into urea via the urea cycle. The remaining ammonia exits the liver via the hepatic veins and is distributed within the circulation. The heart, kidneys, brain, skeletal muscle and intestine can also metabolize ammonia. Ammonia and amino acids are also released into the circulation following muscle damage and, similarly, will be metabolized in the liver. The urea is then excreted through the kidneys. In an animal with liver dysfunction, a urea cycle defect or a portosystemic shunt (PSS), the ammonia is not sufficiently metabolized and enters the systemic circulation and the brain tissues. In the brain, ammonia metabolism produces glutamine as well as urea. This glutamine is degraded to the excitatory neurotransmitter glutamate. Increased brain glutamate will increase neuronal excitability and is one factor in the development of hepatic encephalopathy.**

is >10 cm H_2O. Once the plasma space is adequately volume expanded (normal hydration and capillary refill time <2 seconds), repeated injections of furosemide can be given intravenously to enhance diuresis. Glucocorticoids should not be used to treat hypercalcaemia until a diagnosis is reached since they may worsen some disease processes and hamper the identification of others. Total and ionized calcium, serum phosphate, BUN and creatinine levels should be serially monitored.

Prognosis

PHPTH carries a good prognosis with appropriate therapy. The prognosis for other causes of hypercalcaemia varies considerably, but is often guarded.

Hepatic encephalopathy

Aetiology/pathophysiology

HE is a complex neurological condition that occurs as a consequence of acute or chronic liver disease, most frequently due to congenital portovascular anomalies, hepatic microvascular dysplasia or liver failure from any cause including intoxication or infection. Multiple pathophysiological theories have been proposed and these are briefly discussed here.

Ammonia

Elevated blood ammonia is characteristic of HE, but the role of ammonia in the pathogenesis of HE is controversial since the degree of correlation between HE severity and blood ammonia concentration is variable. The labile nature of blood ammonia may be the origin of much of the inconsistency in the results obtained. Ammonia (NH_3) is produced primarily in the gastrointestinal tract by bacterial metabolism of amino acids, urea and glutamine. NH_3 diffuses through the intestinal mucosa into portal blood and is delivered to the liver as ammonium (NH_4^+) (**386**). The liver itself produces

ammonium ions from amino acid deamination. In liver failure, hepatic ammonia detoxification is ineffective, leading to hyperammonaemia. Ammonium ions are detoxified predominantly in the liver via the urea cycle, with resultant production of glutamine. The brain lacks a urea cycle and relies on production of glutamine for detoxification of ammonia, which is a direct neurotoxin acting via chloride channel inhibition. It has been suggested that the glutamine produced acts as the 'Trojan horse' of HE pathogenesis by inducing oxidative stress. Much of the evidence supporting the ammonia theory comes from the apparent efficacy of anti-ammonia therapies such as lactulose, oral synbiotics, oral antimicrobials and enteral or parenteral L-ornithine–L-aspartate.

GABA/benzodiazepine

GABA is the principal inhibitory neurotransmitter in the CNS and increased GABAergic tone results in impaired motor function and decreased consciousness. The GABAergic theory suggests that HE is due to increased circulating levels of GABA derived from the gastrointestinal tract, although the theory has been modified to include the involvement of endogenous benzodiazepines, which are also increased in HE patients. Activation of the GABA/benzodiazepine receptor complex causes chloride ion influx, membrane hyperpolarization and neuronal inhibition. This theory is supported by the improvement in clinical signs in HE patients given the benzodiazepine receptor antagonist flumazenil, although this drug appears to improve encephalopathic signs in less than half of HE patients.

Aromatic amino acids

The concentrations of branched-chain amino acids in the brain decrease in liver disease, while those of aromatic amino acids increase. This increase in brain aromatic amino acid concentration may lead to false neurotransmitter generation; however, branched-chain amino acid administration does not appear to be effective for treatment of HE.

Manganese

This trace element is an essential constituent of multiple antioxidant metalloenzymes such as superoxide dismutase. Manganese-induced neurotoxicity causes astrocyte dysfunction, neuronal loss and gliosis. Manganese is excreted via the hepatobiliary route and its concentration increases in liver disease. Patients with chronic liver disease and HE have increased brain manganese concentrations, although whether this is causative or coincidental is unknown. Increased manganese concentration may appear as a bright signal on T1-weighted MR images, which has been observed in the lentiform nuclei in a canine patient.

TNF-alpha

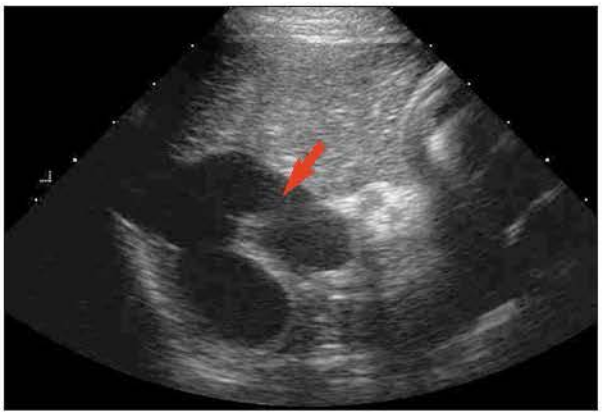
Circulating levels of TNF-α, a proinflammatory cytokine, are increased in liver failure patients and appear to correlate with HE severity. In liver failure, TNF-α production increases while TNF-α clearance may be reduced. Pathological derangements of the brain in HE may be induced in part by TNF-α excess. The TNF-α hypothesis links a number of the other hypotheses together. TNF-α increases CNS endothelial ammonia diffusion, enhances glutamate receptor-mediated neurotoxicity and is associated with significantly increased levels of GABA. Additionally, TNF-α increases peripheral type benzodiazepine receptors and excess manganese potentiates in-vitro production of TNF-α.

Reactive oxygen species/reactive nitrogen species

Oxidative and nitrosative stress may play a role in HE development. Hyperammonaemia, inflammatory cytokines and benzodiazepines induce ROS production. Oxidative stress is linked to astrocyte swelling, a key component of the pathophysiology of HE. Ammonia, TNF-α , benzodiazepines and astrocyte swelling trigger an NO-dependent Zn^{2+} mobilization, which modulates GABA function, peripheral benzodiazepine receptor expression and neurosteroid synthesis. ROS generation and secondary astrocyte swelling may thus mechanistically link the other theories together.

Clinical presentation

HE is well documented in both humans and small animals and is characterized by changes in behaviour, consciousness and NM function. Neurological signs may include head pressing, hyperreflexia, rigidity, myoclonus, seizures and coma. Signs of hepatic dysfunction (weight loss, polydipsia, anorexia and vomiting) may be present. Ptyalism is another common sign, especially in cats.



▲ 387 Ultrasound image of a 7-month-old female Weimaraner through a dorsal right-sided intercostal window demonstrating a large intrahepatic portosystemic shunt. (Photo courtesy Francisco Llabres-Diaz)

Diagnosis

HE is diagnosed primarily by clinical signs in conjunction with biochemical evidence of liver dysfunction. Serum biochemistry evidence of liver dysfunction includes hypoalbuminaemia, hypocholesterolaemia, low BUN and hypoglycaemia. Increased liver enzyme concentrations indicate hepatocellular damage or cholestasis, which are commonly seen in patients with disease processes causing liver dysfunction. Patients with congenital portovascular anomalies commonly have two-to-threefold increases in liver enzymes. Supportive findings from specific liver function tests include hyperammonaemia, increased pre- and/or postprandial bile acids or clotting time prolongations. Microcytosis is an inconsistent haematological finding in liver disease. Abdominal imaging, and in particular ultrasound, may be useful in identifying liver pathology such as biliary tract disease or neoplasia. Identification of a portosystemic shunt is possible by ultrasonography (**387**) or mesenteric portography. MRI of the brain may reveal cortical atrophy characterized by widened sulci, and hyperintensity of the lentiform nuclei on T1-weighted images. Hepatic biopsy is rarely required.

Management

HE therapy has three aims: stop the seizures; reduce serum levels of neurotoxic metabolites; treat the underlying cause.

Stop seizures

If the patient is having seizures, antiepileptic drug treatment will be necessary. Controversy exists over the use of benzodiazepines for treatment of HE-associated seizures; however, they remain the first-line drug of choice. For maintenance therapy, ideally, a drug with no effect on hepatic metabolism should be used. Potassium bromide is theoretically a good choice and it can be given via a loading protocol over 1–6 days either orally or rectally (see Chapter 23). Levetiracetam (20–60 mg/kg) may be effective when given intravenously, intramuscularly or per rectum, although it has not yet been evaluated for efficacy in animals via these routes or at these doses. In patients with SE secondary to HE, it may be necessary to use anaesthetic drugs, some of which have potent anti-seizure properties, in order to terminate seizure activity. Propofol (1–4 mg/kg IV for induction, given to effect followed by CRI 0.1–0.6 mg/kg/minute) can be used for this. Once anaesthesia is induced patients must be intubated to protect their airway and an intensive protocol of monitoring and care of the recumbent patient initiated. (*Note:* Electrical seizure activity may continue despite the appearance of a cessation of tonic or clonic activity.) Other measures to treat HE must also be initiated in patients with SE.

Some patients develop neurological dysfunction following portosystemic shunt ligation. One study reported postoperative neurological abnormalities in 11/89 dogs within 6 days of surgical shunt attenuation. The cause of postoperative seizures is not known. Signs included disorientation, ataxia, generalized seizures and SE. The development of SE following surgical attenuation probably carries a poor prognosis. However, nine of the 11 patients described in this study survived. The authors concluded that perioperative phenobarbital therapy may not prevent such neurological sequelae, but may reduce their severity.

Reduce neurotoxic metabolites

Oral lactulose (0.5–1.0 ml/kg PO q8h) decreases gut transit time, helps to prevent constipation and alters gut flora, thus reducing colonic ammonia production. Once metabolized it produces an acid environment, trapping ammonia as ammonium. In stuporous or comatose patients, lactulose can be administered by retention enema (20 ml/kg, made of three parts lactulose diluted in seven parts warm water, q4–6h).

Ampicillin (22 mg/kg PO q8h) or, if unavailable, metronidazole (7.5 mg/kg PO q8h) or neomycin (20 mg/kg PO q8h) can be used to reduce urea-splitting colonic bacterial numbers. Proximal gastrointestinal haemorrhage may exacerbate encephalopathic signs and should be treated with proton-pump inhibitors such as omeprazole. This drug can be given orally or intravenously (1 mg/kg). Additionally, gastrointestinal bleeding in patients with liver dysfunction must be investigated to identify any underlying thrombocytopenia or coagulopathy that requires specific treatment.

If appropriate, based on the patient's mentation, the diet may be altered to a high-quality, low-protein one to reduce ammonia production in the gastrointestinal tract. Care must be taken not to limit protein intake excessively since many patients with portovascular anomalies are young, growing patients and such protein restriction may be detrimental to their musculoskeletal development.

Treat underlying cause

Surgical ligation of single, uncomplicated extrahepatic or intrahepatic shunts is the most direct treatment. Dogs and cats with multiple extrahepatic shunts and those with acquired shunts secondary to cirrhosis or acute fulminant hepatic failure are not candidates for surgery. In cases of acquired liver disease, specific therapy for any underlying cause should be instituted.

Prognosis

The prognosis for dogs and cats with HE is dependent on the degree of hepatic impairment and the severity of the neurological signs. It is guarded in patients with seizures secondary to HE, poor in patients with liver failure and fair with surgical treatment in patients with portovascular anomalies.

Hypoglycaemia

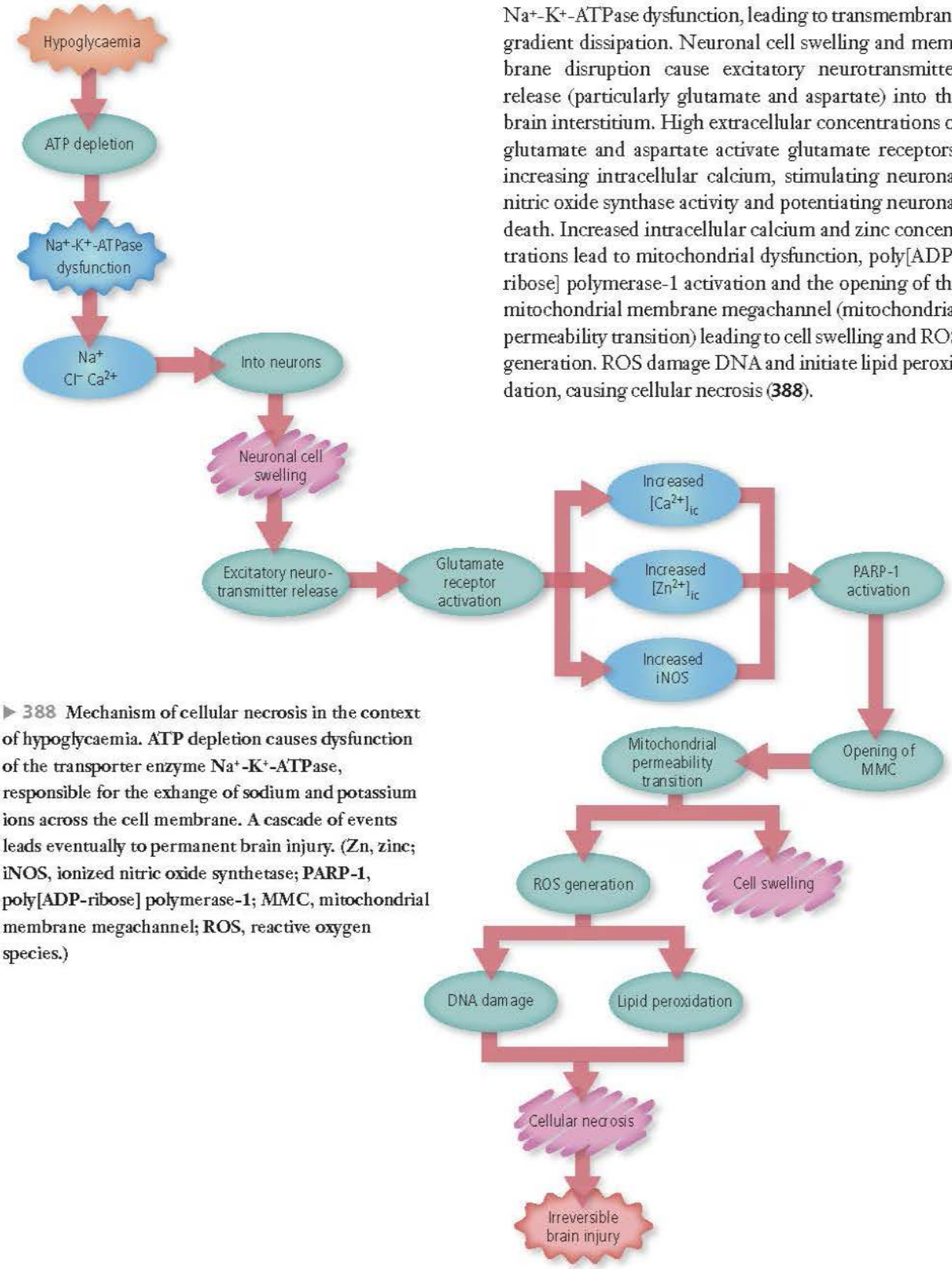
Aetiology/pathophysiology

Hypoglycaemia may arise from numerous conditions. Hypoglycaemic neurological dysfunction has been reported in patients with endogenous and iatrogenic hyperinsulinaemia, sepsis, liver failure, portosystemic shunting, hypoadrenocorticism, neoplasia (insulinoma or extrapancreatic insulin-like producing neoplasm), neonatal hepatopathy and xylitol toxicity. Hypoglycaemic neurological dysfunction is also reported in toy breeds and in hunting dogs.

Despite constituting only 2% of total body mass, the brain utilizes 25% of total body glucose due to its inherently high metabolic rate and limited local storage. Brain interstitial glucose concentrations are typically 20–30% less than plasma, therefore glucose must be continuously transported into the brain. Blood glucose is closely monitored by glucose-sensing neurons in the hypothalamic ventromedial nuclei. Hypoglycaemia stimulates these neurons, leading to increased sympathetic output and, therefore, increased plasma epinephrine (adrenalin), norepinephrine (noradrenalin), cortisol, glucagon and somatostatin concentrations. These counter-regulatory hormones act to increase plasma glucose concentration, increase glucose delivery to, and uptake by, the brain and alter glucose metabolic pathways. Insulin is not required for glucose uptake by the brain because of specific glucose transporting transmembrane proteins.

If hypoglycaemia persists and mechanisms to increase glucose delivery and uptake are inadequate, the brain can shift towards production of pyruvate via glycolysis, which is then shuttled to lactate. Astrocyte mobilization of glycogen stores and subsequent lactate production provides a limited energy supply for neurons. Brain glycogen stores appear to be consumed gradually during hypoglycaemia. The exhaustion of these stores seems to coincide with ATP depletion and the onset of EEG isoelectricity, suggestive of neuronal death and potentially irreversible brain injury. It also seems that brain function becomes impaired before ATP depletion is detectable, concomitant with changes in brain monoamine concentrations, increased free fatty acid concentration and impaired plasma membrane function. At the point of energy failure, where brain glucose has fallen by >97%, ATP becomes abruptly depleted. ATP depletion causes

Na^+-K^+-ATPase dysfunction, leading to transmembrane gradient dissipation. Neuronal cell swelling and membrane disruption cause excitatory neurotransmitter release (particularly glutamate and aspartate) into the brain interstitium. High extracellular concentrations of glutamate and aspartate activate glutamate receptors, increasing intracellular calcium, stimulating neuronal nitric oxide synthase activity and potentiating neuronal death. Increased intracellular calcium and zinc concentrations lead to mitochondrial dysfunction, poly[ADP-ribose] polymerase-1 activation and the opening of the mitochondrial membrane megachannel (mitochondrial permeability transition) leading to cell swelling and ROS generation. ROS damage DNA and initiate lipid peroxidation, causing cellular necrosis (**388**).



▶ **388** **Mechanism of cellular necrosis in the context of hypoglycaemia. ATP depletion causes dysfunction of the transporter enzyme Na^+-K^+-ATPase, responsible for the exhange of sodium and potassium ions across the cell membrane. A cascade of events leads eventually to permanent brain injury. (Zn, zinc; iNOS, ionized nitric oxide synthetase; PARP-1, poly[ADP-ribose] polymerase-1; MMC, mitochondrial membrane megachannel; ROS, reactive oxygen species.)**

Clinical presentation

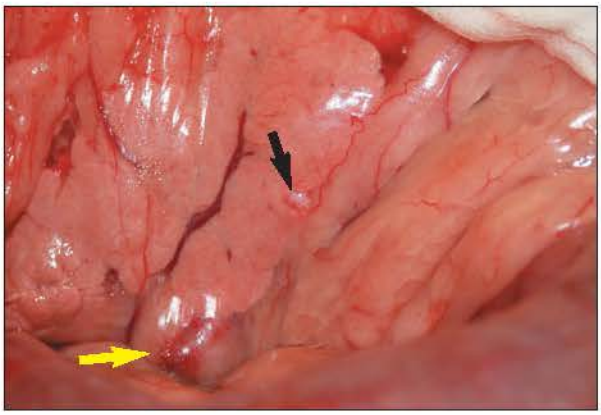
Clinical signs of cortical neuronal damage range from hyperexcitability to tremors, blindness, cognitive dysfunction, seizures, coma and death. Nervousness, tremors and weakness typically appear when plasma glucose levels approach 3.6–3.8 mmol/l (64.8–68.4 mg/dl). When plasma glucose levels fall below 1 mmol/l (18 mg/dl), seizures, severe brain damage, coma and death may occur. However, as with many homeostatically controlled parameters, the rate of change may be more important than the absolute values in determining the point of onset and severity of clinical signs. Early recognition and therapy for hypoglycaemia are vital both for early return of neuronal function and to diminish the risk of permanent damage.

Diagnosis

A blood glucose measurement that is consistently less than the reference interval is diagnostic of hypoglycaemia. (*Note:* False hypoglycaemia may result from use of human point-of-care glucometers in haemoconcentrated patients.) Falsely low glucose values may also result from delayed separation of serum from RBCs as these cells continue to consume glucose for glycolysis. This can be prevented by using a sodium fluoride tube. Once hypoglycaemia is identified, a thorough investigation for an underlying cause must be undertaken. Principle rule-outs include sepsis, liver failure, hypoadrenocorticism, insulin overdose, xylitol toxicity, neonatal or toy breed hypoglycaemia, insulinoma (**389**) and other paraneoplastic hypoglycaemias.

Management

The underlying cause of the hypoglycaemia must be addressed. An intravenous dextrose bolus (0.5 g/kg 50% dextrose diluted 1:4 with 0.9% saline) should be given and continued with a CRI of 2.5–5% dextrose in an isotonic fluid as required to maintain normoglycaemia. Solutions of 2.5–5% dextrose can be readily prepared by adding aliquots of a solution of 50% dextrose to 0.9% saline or Hartmann's solution (e.g. 50 ml of 50% dextrose in 500 ml saline creates a 5% solution). Glucose syrup can be administered orally if intravenous access is not available; however, there needs to be caution using the oral route if the patient is actively seizuring. Frequent small meals should be fed throughout the day.



▲ **389** **Intraoperative image of an insulinoma, which is a few millimetres across (black arrow) within the left limb of the pancreas. A local lymph node appears enlarged (yellow arrow). Histopathology of this affected lymph node confirmed the presence of metastasis from the insulinoma. (Photo courtesy Ronan Doyle)**

Renal failure

Aetiology/pathophysiology

Patients with acute or chronic renal failure may develop encephalopathy due to uraemia, thiamine deficiency, dialysis, transplant rejection, hypertension, fluid and electrolyte disturbances or drug toxicity. Uraemic encephalopathy is typically more severe in patients with acute renal failure. The pathophysiology of this encephalopathy is complex and poorly understood, but metabolite accumulation, hormonal disturbances, metabolic abnormalities and neurotransmitter imbalances may all contribute. Renal failure results in accumulation of numerous organic substances that possibly act as uraemic neurotoxins, but no single metabolite has been identified as the sole cause of uraemia and the degree of azotaemia correlates poorly with the degree of neurological dysfunction. Accumulation of urea, guanidine compounds, uric and hippuric acids, amino acids, polypeptides, polyamines, phenols, phenolic and indolic acids, acetone, glucuronic acid, carnitine, myo-inositol, sulphates, phosphates and middle molecules has been reported. NMDA receptor activation and concomitant inhibition of $GABA_A$ neurotransmission have also been proposed.

Hormonal disturbances, particularly PTH, have been suggested to play a role in the pathogenesis of uraemic encephalopathy. PTH may facilitate calcium entry into tissues, altering the brain calcium balance and disrupting cerebral function. Thiamine deficiency in uraemic patients is rare, although dialysis patients are at increased risk. Encephalopathy due to aluminium accumulation secondary to use of aluminium-based phosphate binders has been reported in humans and in dogs.

Systemic hypertension commonly accompanies renal failure. Chronic systemic hypertension has a variety of pathological consequences, which is referred to as end-organ or target organ damage (TOD). Important TOD is observed in the kidneys, eyes, heart and nervous system. Hypertensive encephalopathy is thought to be caused by vasogenic oedema due to impaired cerebrovascular autoregulation, endothelial injury and elevated plasma natriuretic peptide concentrations. With acute hypertension, the autoregulatory capacity of the brain vasculature may be exceeded, which leads to hyperperfusion, breakdown of the blood–brain barrier and cerebral oedema. In chronic hypertension, brain vasculature may be chronically vasoconstricted, leading to hypertrophy and hyperplasia of the smooth muscle. As a result, fibrous changes develop allowing leakage of plasma, which ultimately causes degeneration of the vasculature, predisposing to vessel rupture and microhaemorrhages. Clinically, it is associated with lethargy, ataxia, blindness, stupor and seizures.

Fluid and electrolyte disturbances, including hypercalcaemia, hypo- and hypernatraemia and hypo- and hyperosmolality, are common in patients with renal failure and may contribute to encephalopathy. Encephalopathy may also occur due to drug accumulation secondary to renal insufficiency. Drugs implicated include metronidazole and cefazolin. Additionally, altered drug–protein binding in renal failure may lead to neurotoxicity associated with theophylline, diazepam, propranolol and cimetidine.

Diagnosis

Serum biochemical analysis demonstrates very severe azotaemia, hyperphosphataemia ± accompanying alterations in total and ionized calcium levels. Urinalysis before fluid therapy showing isosthenuria is compatible. Systemic hypertension and a non-regenerative anaemia are common in chronic renal failure patients. Investigations must be directed towards identifying any reversible underlying cause.

Management

Reversible conditions (e.g. ureteric obstruction) should be identified and treated. Fluid balance and electrolyte disturbances are corrected with targeted fluid therapy (see Chapter 31). If the patient is anuric, an attempt should be made to establish urine output with fluid therapy and osmotic or loop diuretics. This should be monitored for signs of fluid overload. If the patient is polyuric, diuresis should be provided.

Systemic hypertension should be monitored and treated if systolic BP is >200 mmHg, mean >140 mmHg or diastolic BP is >110 mmHg, or if signs of end-organ damage exist (e.g. retinal haemorrhage). ACE inhibitors (e.g. benazepril, 0.25–0.5 mg/kg PO q24h in the dog or 0.25–1.0 mg/kg PO q24h in the cat; amlodipine, 0.1 mg/kg PO q24h; or hydralazine, 0.5–2.0 mg/kg PO q12h in the dog or 2.5 mg/cat PO q12h) are the drugs of choice.

If renal failure is severe, or patients remain anuric, peritoneal dialysis and haemodialysis are the only options available to reduce azotaemia. Referral for dialysis should be considered, but the clinician must be aware of dialysis disequilibrium syndrome (DDS) in severely azotaemic patients. DDS is a CNS disorder that is an important clinical problem in human dialysis patients. It is characterized by neurological symptoms of varying severity that are thought to be due primarily to cerebral oedema. Predisposing factors include severe metabolic acidosis, older age, paediatric patients and the presence of other

CNS disease such as a pre-existing seizure disorder. Classic human DDS refers to acute symptoms developing during or immediately after haemodialysis. Early findings include headache, nausea, disorientation, restlessness, blurred vision and asterixis. More severely affected patients progress to confusion, seizures, coma and even death. It is now recognized that many milder signs and symptoms associated with dialysis, such as muscle cramps, anorexia and dizziness developing near the end of a treatment, are also part of this syndrome.

Prognosis

Patients with uraemic encephalopathy are typically in end-stage chronic renal failure or are anuric due to an acute renal insult. Anuric patients have a poor prognosis even with haemodialysis.

Table 92 **Canine systemic inflammatory response criteria**

* Rectal temperature	≤37.8°C or >39.7°C (≤100.0°F or >103.5°F)
* Heart rate	≥160 bpm
* Respiratory rate	≥40 breaths/minute
* Leucocyte count	<4 x 10^9/l or >12 x 10^9/l WBCs or band neutrophils >10%

*3 out of 4 are necessary

(Adapted from Okano S, Yoshida M, Fukushima U *et al.* (2002) Usefulness of systemic inflammatory response syndrome criteria as an index for prognosis judgement. *Vet Rec* **150:**245–246.)

Sepsis

Overview

Sepsis-associated encephalopathy (SAE) is a well-recognized, although ill-defined, entity in humans, occurring in 23% of patients in one study. Definitive identification of the condition is problematic because few criteria are both sensitive and specific. To date, SAE has not been reported as a specific entity in small animals. Given the similarities between canine and human sepsis it is probable that dogs also suffer from SAE. SAE associated with gram-negative sepsis appears to have a higher mortality in people. Septic encephalopathic patients have significantly higher mortality than those with normal mentation. Pathologically, the cerebrum is most commonly involved. Multiple lesion types have been described including ischaemic lesions, particularly in autonomic nuclei, purpura, central pontine myelinolysis, multifocal necrotizing leucoencephalopathy, haemorrhage, microabscessation, perivascular oedema and disruption of astrocyte foot processes. Neuronal damage includes eosinophilic cytoplasm, shrunken nuclei and disruption of the nuclear membrane. Astrogliosis and focal necrosis of cerebral white matter have been described in experimental neonatal kittens following intraperitoneal injection of *E. coli* lipopolysaccharide.

Aetiology/pathophysiology

SAE pathophysiology is incompletely understood and is probably multifactorial. Brain dysfunction in sepsis may be related to microbial toxins, inflammatory mediators, metabolic and vascular abnormalities, mitochondrial dysfunction, oxidative stress and apoptosis. Bacterial toxins can exert CNS effects and induce brain dysfunction. Endotoxin-induced inflammatory mediators and ROS cause endothelial, astrocyte and neuronal dysfunction. Plasma and CSF concentrations of ascorbate are significantly reduced in encephalopathic septic patients. Endotoxin interferes with the hypothalamic–pituitary axis. Breakdown and enhanced permeability of the blood–brain barrier have been observed in SAE, leading to alterations in cerebral monoamine concentrations and perivascular oedema formation. In patients with SAE, altered mental status has been related to aromatic amino acid excess and decreased levels of branched-chain amino acids.

Table 93 **Feline systemic inflammatory response criteria**

* Rectal temperature	≤37.8°C or >39.7°C (≤100.0°F or >103.5°F)
* Heart rate	<140 bpm or >225 bpm
* Respiratory rate	>40 breaths/minute
* Leucocyte count	<5 x 10^9/l or >19.5 x 10^9/l WBCs or band neutrophils >5%

*3 out of 4 are necessary

(Adapted from Brady CA, Otto CM, Van Winkle TJ *et al.* (2000) Severe sepsis in cats: 29 cases (1996–1998). *J Am Vet Med Assoc* **217**:531–535.)

Diagnosis

Sepsis is defined as the systemic inflammatory response to infection. Sepsis is diagnosed on the basis of positive systemic inflammatory response criteria (*Tables 92* and *93*) with suspected or confirmed infection. SAE should be considered in any patient with sepsis who develops clinical signs of encephalopathy. SAE should be considered a diagnosis of exclusion and efforts should be made to exclude other potential causes of metabolic encephalopathy such as hypoglycaemia. Confirmation of characteristic pathological findings requires postmortem examination.

Management

No specific treatment for SAE exists. Once sepsis is diagnosed, treatment should focus on cardiovascular system support, rapid initiation of appropriate intravenous antimicrobials, source control if appropriate and close patient monitoring.

Prognosis

Sepsis itself carries a guarded to poor prognosis, with reported mortality rates varying between 20% and 70% in small animals. It is likely that SAE will only occur in those most severely affected and therefore the prognosis is probably worse for this patient population.

THERMOREGULATORY DISORDERS

Heatstroke

Overview

Heatstroke, the most severe form of heat-induced illness, has been defined as hyperthermia associated with a systemic inflammatory response leading to a syndrome of multiorgan dysfunction in which encephalopathy predominates.

Aetiology/pathophysiology

Heatstroke occurs when the thermal load exceeds the patient's ability to dissipate heat and can be exertional or non exertional. The degree of injury is dependent on both the magnitude and duration of core temperature increase. Direct thermal injury and protein denaturation occur at approximately 42.8°C (109.0°F). Experimental evidence suggests that sustained temperatures as high as 40.6°C (105.1°F) may cause permanent brain damage, although recovery is possible even when the temperature reaches 46.5°C (115.7°F). Severe hyperthermia results in massive neuronal injury and cell death. Cerebral oedema, haemorrhage, infarction and cerebellar dysfunction are common consequences of severe hyperthermia in dogs. Although the exact mechanisms are unclear, dopamine, serotonin, glutamine and cytokines (e.g. IL-1, IL-6, TNF-α) have been implicated as potential mediators. The development of cerebral and cerebellar oedema and localized areas of necrosis due to intracranial haemorrhage can lead to disorientation, seizures, coma and sometimes death. Excessive temperatures in the hypothalamus may impair temperature regulation by damaging the thermoregulatory centre. Arterial hypotension and cerebral ischaemia may also be involved in the development of canine heatstroke.

Management

Hyperthermia must be distinguished from pyrexia through assessment of the patient's history, signalment, physical examination findings and clinicopathological data. Major body system abnormalities should be identified and treated as appropriate and oxygen provided. Room temperature intravenous fluids should be given as required to correct hypoperfusion. Sedation may be necessary to reduce stress. Only sedative agents with

minimal effects on the cardiopulmonary system should be used in patients with heatstroke who may be suffering from shock (see Chapter 29).

Active cooling must be undertaken if the body temperature is >39.5°C (>103.1°F). This can be achieved by dousing the fur with tepid water and blowing air across the patient. In extreme cases where the body temperature is >42°C (>107.6°F), additional measures, such as cool water enemas or peritoneal lavage (10–20 ml/kg room temperature sterile saline), may be required, although experimental studies suggest that evaporative cooling may be as effective as peritoneal lavage. Ice water must not be used since this may cause vasoconstriction, reducing efficacy and potentially inducing shivering. Corticosteroids or NSAIDs should not be administered. They will not reduce the patient's temperature and are contraindicated in patients with shock or gastrointestinal injury. Aggressive cooling efforts should be discontinued when the patient's temperature reaches 39.5°C (103.1°F) to prevent overshoot hypothermia, which might be detrimental.

Hypothermia

Aetiology/pathophysiology

Primary hypothermia results from exposure to low environmental temperatures, while the causes of secondary hypothermia are multifactorial and include underlying disease, trauma, toxins, immobility, surgery and anaesthesia. Primary hypothermia in dogs and cats is classified as mild 32–37°C (89.6–98.6°F), moderate 28–32°C (82.4–89.6°F), severe 20–28°C (68.0–82.4°F) and profound <20°C (<68°F). A different correlation exists between body temperature and clinical signs associated with secondary hypothermia, where comparable adverse effects occur at higher temperatures. For secondary hypothermia, mild is classified as 36.7–37.7°C (98.1–99.9°F), moderate as 35.5–36.7°C (95.9–98.1°F), severe as 33–35.5°C (91.4–95.9°F) and critical <33°C (<91.4°F). Controlled hypothermia following return of spontaneous circulation after cardiopulmonary arrest may be neuroprotective. Severe CNS depression and coma may occur with progressive hypothermia. Mild-to-moderate hypothermia reduces CBF and impairs cerebral autoregulation. Cerebrovascular autoregulation is lost below ~25°C (77°F) and in addition, CBF decreases by 6–7% for each 1°C drop in body temperature. However, in severe hypothermia there is a markedly reduced metabolic rate, conferring increased cerebral ischaemic tolerance. The EEG becomes flat at body temperatures below ~20°C (68°F) in people.

Management

For mild hypothermia, passive external rewarming with blankets to prevent further heat loss is appropriate. For moderate hypothermia, active external rewarming is appropriate. A forced air blanket is ideal. Direct application of heat sources to skin must be avoided. External rewarming should be applied to the trunk and head, not to the extremities. For severe hypothermia, active core rewarming by peritoneal lavage should be considered in addition to other techniques. (*Note:* Beware of rewarming shock [hypotension due to vasodilation] and afterdrop [falls in core temperature due to peripheral vasodilation] during treatment.)

Thiamine deficiency

Overview

Vitamin B_1 (thiamine) is an essential dietary component in small animals. Thiamine pyrophosphate is a coenzyme for pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase and transketolase, all of which are involved in carbohydrate metabolism. Thiamine deficiency impairs oxidation of ketoacids, leading to impaired cerebral energy metabolism, focal lactic acidosis, NMDA receptor-mediated excitotoxicity and blood–brain barrier breakdown.

Clinical presentation

Thiamine deficiency, termed Wernicke's encephalopathy in people, causes polioencephalomalacia with bilaterally symmetrical spongiosis, necrosis and brainstem nuclei haemorrhage. Thiamine-deficient dogs present with dilated unresponsive pupils and mild ataxia progressing to altered mentation, hyperaesthesia, tetraparesis, seizures and opisthotonus. Cats, in contrast, display central vestibular signs, head tremors, mydriasis and cervical ventroflexion. Thiamine deficiency in dogs and cats has been reported secondary to feeding of sulphur dioxide-preserved meat, feeding thiamine deficient diets or fresh fish diets containing thiaminase. Thiamine deficiency can occur due to decreased intake, impaired absorption due to intestinal disease, liver dysfunction, increased utilization secondary to fever or infection or increased urinary loss.

Diagnosis

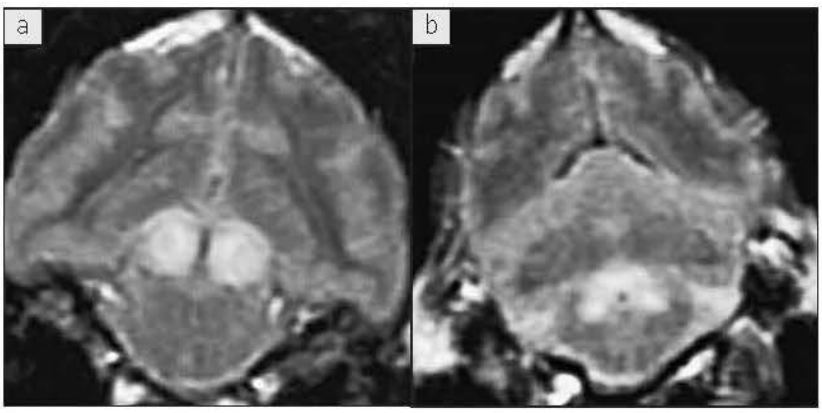
Diagnosis of thiamine deficiency is typically made on the basis of signalment, clinical signs and a detailed dietary history. Confirmation of the deficiency can be made by assays of thiamine metabolites in blood or by measurement of erythrocyte transketolase activity. Presumptive diagnosis can be made on the basis of urinary organic acid profile analysis. Occasionally, a diagnosis is only confirmed postmortem. Clinical sign resolution following treatment with thiamine is supportive of the diagnosis. CSF analysis does not appear to be discriminatory for thiamine deficiency. MRI findings have been described in the dog and cat including non-contrast enhancing bilaterally symmetrical thalamic and brainstem nuclear hyperintensity evident on T2-weighted and FLAIR images (**390**).

Management

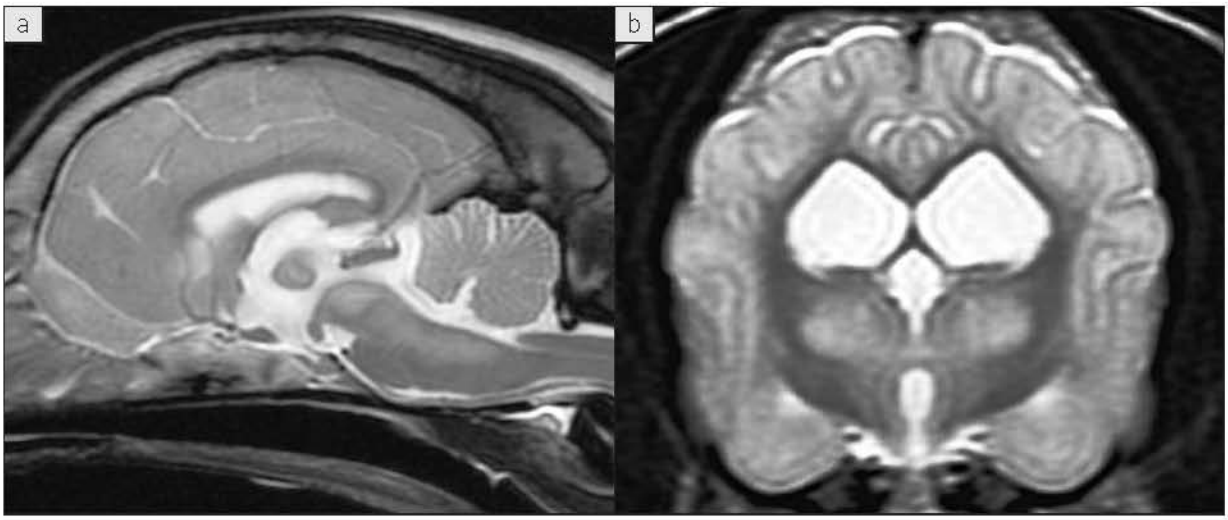
Thiamine deficiency can be treated with thiamine hydrochloride (5–50 mg/dog IV, IM or PO q24h or 1–20 mg/cat by slow CRI). The underlying disorder should also be investigated and managed appropriately.

Prognosis

Provided the diagnosis is made early or presumptive treatment is rapidly initiated, then the prognosis for thiamine deficiency is good.



◀ **390** Transverse T2-weighted FLAIR MR images of a Cocker Spaniel with thiamine deficiency. There is bilaterally symmetrical hyperintensity at the level of the rostral colliculus (a) and vestibular nuclei (b).



▲ **391** Sagittal (a) and transverse (b) T2-weighted MR images of a Staffordshire Bull Terrier with L-2-hydroxyglutaric aciduria. There is diffuse abnormal hyperintensity extending rostrally through the dorsal brainstem to the thalamus and also affecting the grey matter of the cerebellum and cerebral hemispheres (a). Note the symmetrical hyperintensity in the grey matter of the cerebral hemispheres and the thalamus (b).

Inborn errors of metabolism

Organic acidopathies: L-2-hydroxyglutaric aciduria

Overview

L-2-hydroxyglutaric aciduria is an inherited disease of Staffordshire Bull Terriers and West Highland White Terriers. It is an organic acidopathy characterized by raised L-2 hydroxyglutaric acid in plasma, urine and CSF.

Clinical presentation

The condition has an acute or chronic onset and it is progressive over 4 months to 7 years. Clinical signs include seizures, ataxia, head tremor and subtle behaviour changes/dementia.

Diagnosis

Bilateral symmetrical hyperintensity is evident on T2-weighted MR images of the cerebral, cerebellar, thalamic and brainstem grey matter (**391**). CSF cytology and protein content are normal. L-2-hydroxyglutaric acid levels are increased in urine, plasma and CSF.

A causative mutation in the canine homologue of the L-2-hydroxyglutarate dehydrogenase gene has been identified. A genetic test is available commercially at the Animal Health Trust, Newmarket, UK. Histopathology reveals diffuse polioencephalopathy.

Management

Treatment is palliative and symptomatic (e.g. antiepileptic drugs).

Prognosis

The prognosis is poor, although some dogs can be managed symptomatically for many months to years.

NEUROLOGICAL TOXICITIES

Jennifer Pittman, Ben Brainard & Katrin Swindells

INTRODUCTION

Neurotoxicity is commonly encountered in emergency veterinary practice. Toxins that cause neurological signs may be exogenous or endogenous in origin. Exogenous neurotoxins include plant and environmental toxins, envenomations, pesticides, herbicides, medications and food. Endogenous neurotoxins are the result of metabolic diseases or organ dysfunction (e.g. hepatic or uraemic encephalopathies) and are not discussed in this chapter (see Chapter 27).

Most toxins affect the neurological system directly; some may have indirect effects due to the metabolic effects of the toxin (e.g. HE due to a toxin that causes hepatic failure). Toxins that have indirect effects on the neurological system will not be covered in depth in this chapter, but they should remain on the veterinarian's differential diagnosis list where applicable. This chapter will discuss the general management of exogenous neurotoxicity. In addition, common toxins will be discussed with reference to mechanism of action, clinical signs, treatment (if available) and prognosis.

GENERAL TREATMENT PRINCIPLES

The main principles of treating neurotoxicity include the following and are often performed simultaneously: systemic stabilization; symptomatic treatment; decontamination and prevention of absorption of further toxins; providing antidotes if available.

Systemic stabilization

The patient's airway should be protected using a cuffed endotracheal tube if the patient is obtunded and/or at risk of aspiration of gastric contents. Suction of the oropharynx with a Yankauer suction tip (**392**) may be necessary in patients who are unable to swallow. (These patients may be more easily anaesthetized and intubated instead of frequent oropharyngeal suctioning.) Patients should be intubated and ventilated if respiratory paralysis or other causes of hypoventilation are present and oxygen should be provided if the patient is cyanotic or hypoxaemic (for further details see Chapter 2).

Maintenance of adequate BP is essential for hepatic and renal perfusion, which are important for the clearance of many toxins. Systemic BP should be measured and normalized, and cardiac arrhythmias should be evaluated and treated. BP may initially be measured using indirect methods (e.g. Doppler probe or oscillometric machine); normal MAP should be near 75 mmHg and normal Doppler blood pressure should be >80 mmHg. Cardiac rhythm may be assessed using electrocardiography or by simultaneous palpation and auscultation for pulse deficits. Techniques for fluid resuscitation of the hypotensive neurological patient are covered in Chapter 31.

Symptomatic treatment

Treatment of neuroexcitatory signs

(See Chapters 13 and 23 for additional discussion, drug doses and administration rates.)



▲ **392** **A Yankauer suction tip may be useful for clearing secretions from the oropharynx.**

Diazepam or midazolam is the first-line therapy for seizures of unknown cause including toxicities. Occasionally, benzodiazepine drugs can result in disinhibition and worsening of hyperaesthesia in susceptible patients. If benzodiazepines are ineffective at stopping seizure activity, phenobarbital may be used. If these drugs are ineffective, anaesthesia may be induced with propofol or alfaxalone. In these cases it is imperative to maintain a protected airway with a cuffed endotracheal tube. Patients who require prolonged anaesthesia can be maintained with volatile anaesthetics (isoflurane, sevoflurane), intravenous infusions of propofol or alfaxalone or intermittent injections or CRIs of pentobarbital, where this is available as a sterile solution for infection. Long-term alfaxalone administration may result in accumulation in cats and requires gradual dose reduction in this situation. Patients with severe muscle tremors, but not seizures, are often best managed with methocarbamol, although benzodiazepines may also be used to provide some muscle relaxation.

Control of body temperature

Patients with hyperthermia (rectal temperature ≥40°C [104°F]) should be aggressively cooled until the rectal temperature is 39.7°C (103.5°F). Convective cooling is the most effective way to cool a patient and involves wetting the fur and placing the animal near a fan.

Application of alcohol to the paw pads is usually not adequate for cooling of hyperthermic patients, and direct application of ice packs may cause cutaneous vasoconstriction and, paradoxically, slow cooling. The application of wet towels to the animal will also slow cooling by impairing evaporative losses. Patients who have been hyperthermic for prolonged periods of time may develop and require treatment for heat stroke, in addition to their primary neurological problem.

Patients presenting with hypothermia should be warmed gradually, with frequent reassessment of temperature, electrocardiography and BP, in addition to metabolic state (e.g. blood glucose concentration). Forced warm air is the most effective way to warm a hypothermic patient and many commercial products are available that may be used for this purpose. Circulating warm water blankets may also be used, but are less effective than forced warm air.

Maintenance of hydration and normovolaemia

Following fluid resuscitation, hydration may be maintained with any isotonic crystalloid fluid (e.g. Normosol R, lactated Ringer's solution or Plasma-Lyte® 148). In addition to maintenance needs, the effect of additional administered drugs (e.g. diuresis by mannitol or furosemide) must be taken into account. Animals with diarrhoea or vomiting, or those that are panting excessively, may have iso or hypotonic fluid losses that must be accounted for. If animals are anaesthetized for long periods of time, free water loss from the respiratory mucosa may occur, especially if the ventilator circuit is not humidified. In addition, the use of sorbitol or other cathartics may result in fluid loss, and the use of propylene glycol-containing activated charcoal suspension may result in serum hyperosmolarity and metabolic acidosis. (Additional information about fluid therapy in the neurological patient can be found in Chapter 31.)

General nursing care

Recumbent animals should be turned every 4 hours and maintained on padded bedding to prevent pressure sores and muscle damage. Recumbent animals are also at risk for atelectasis and subsequent hypoxaemia; this may be prevented by supporting these patients in sternal recumbency if possible, and oxygenation should be monitored regularly. Daily physiotherapy of limbs is indicated for animals that will have a prolonged period of recumbency (see Chapter 32). If the animal is unable to void urine, bladder management protocols should involve regular expression or catheterization to prevent overdistension of the urinary bladder. Animals with paralysis may also be unable to blink. If this occurs, lubricants, such as hyaluronan, petroleum-based lubricants or artificial tears, should be applied at least every 4 hours.

Decontamination and prevention of absorption of further toxin

The methods used to prevent absorption of toxins, as well as those used for decontamination, will depend on the route of entry of the toxin and the metabolic profile of the toxin. Many methods both decrease absorption as well as decontaminate by encouraging elimination of the toxin.

Cutaneous toxins

Most toxins that are absorbed by a cutaneous route are lipid soluble. It is important to ensure that the patient is physiologically stable prior to bathing. Washing-up liquid may be more effective than shampoo at removing fats and lipids. Multiple baths may be necessary to fully decontaminate the animal. Detergents should not be used and medicated shampoos should be avoided. Persons handling animals should wear gloves for their own safety while washing off cutaneous toxins.

Inhaled toxins

Patients should be removed from the toxic atmosphere to a well-ventilated area and oxygen should be provided if indicated. Animals that have inhaled caustic substances may require mechanical ventilation and aggressive supportive care.

Gastrointestinally absorbed toxins

Decontamination methods consist of emesis, gastric lavage and colonic lavage. Activated charcoal and/or cathartics can be used to decrease absorption of toxins.

Emesis

Emesis is most successful within 2 hours of toxin ingestion and rarely successful if >6 hours after ingestion. Vomiting should continue until vomition is no longer productive to optimize gastric content evacuation. For rapidly absorbed or small volume ingestions, and for exposures that occurred beyond the 4–6 hour window, administration of activated charcoal is a more effective method of decontamination. Emesis is generally contraindicated in cases of ingestion of caustics (risk of worsening oesophageal injury), hydrocarbons or other volatile substances (high risk of pulmonary aspiration). It is also contraindicated in animals with obtundation, pharyngeal paresis/paralysis, dysphagia or seizures due to an inability to protect the airway during emesis. (See *Table 94* for commonly used emetic agents.)

Table 94 **Commonly used emetic agents**

- **Apomorphine**
  - 0.04 mg/kg IV or 0.06 mg/kg SC or IM
  - 0.25 mg/kg of crushed tablet may be placed into the conjunctival sac
  - If administered subconjunctivally, eye should be rinsed with artificial tear solution after vomiting
  - If profound depression results, reverse with naloxone (0.04 mg/kg IV, IM, SC)
  - Less effective in cats
- **Xylazine**
  - 0.4 mg/kg SC or IM in cats
  - Sedation may be reversed with yohimbine (0.25–0.5 mg/kg IM) or atipamezole (0.03–0.05 mg/kg SC, IM)
- **Hydrogen peroxide (3%)**
  - 1–2 ml/kg PO up to two times
  - Effective for at-home induction of emesis
- **Sodium carbonate (washing soda crystals)**
  - 1 cm^3 (1 teaspoon) per 20 kg body weight PO
  - A relatively mild emetic, useful for at-home emesis
  - Clinically it is safe so long as not repeatedly dosed
  - Acts as a mild gastric irritant
  - Caution should be exercised to prevent accidental aspiration of this product when administered by inexperienced individuals
  - DO NOT confuse washing soda with caustic soda, which will cause severe oropharyngeal chemical burns
- **Table salt**
  - The administration of large amounts of oral table salt is not a recommended method for induction of emesis due to dangers of acute hypernatraemia and lack of guaranteed efficacy
- **Syrup of ipecac**
  - Syrup of ipecac is not recommended because of the potential for arrhythmias due to cardiotoxicity if emesis does not occur

Gastric lavage

Gastric lavage is used when the patient's condition contraindicates emesis (e.g. profound CNS depression or severe neuroexcitatory signs), but a significant volume of toxin is likely to still be present in the stomach. Generally, it should be performed within 2 hours of toxin ingestion; however, with large-volume toxin ingestions, or those that slow gastrointestinal (GI) motility, it may be productive up to 6 hours postingestion. Gastric lavage is contraindicated in cases of: ingestion of caustics and hydrocarbons; small-volume toxin, which could be decontaminated with activated charcoal; and moderate volume of toxin ingested more than 2 hours previously

Table 95 **Procedure for gastric lavage**

1 Induce anaesthesia with a short-acting intravenous agent such as propofol or alfaxalone. The animal should be in sternal recumbency with the head elevated and pressure applied to the cricoid cartilage until it is intubated and the endotracheal cuff is inflated to minimize the risk of aspiration. Recheck the endotracheal cuff seal frequently during the lavage process, especially when turning the animal.

2 Maintain anaesthesia with gaseous anaesthetic (e.g. isoflurane, sevoflurane) or intravenous infusion of propofol (0.1–0.6 mg/kg/min). These patients are high general anaesthetic risks and require careful monitoring of respiratory and cardiovascular function and anaesthetic depth. A light plane of anaesthesia is adequate as the process is not painful.

3 Maintain body temperature. Unless the patient is hyperthermic, use lavage fluids at body temperature and minimize external heat loss.

4 Protect the airway. Any water present in the pharynx can enter the upper airway and leak past the endotracheal cuff. The patient should be placed in lateral recumbency with the head lower than the rest of the body during lavage.

5 Pre-measure a large-diameter tube (horse/foal stomach tube) from the nose to the last rib and mark the tube at this length with tape. Use the largest tube that can safely be passed.

6 Lubricate and pass the tube gently down the oesophagus to the stomach. A single-lumen tube can be used for both ingress (pouring in warm water) and egress (draining). Alternatively, double-lumen tubes or two smaller tubes can be used. With double tubes, ingress and egress can occur continuously. The stomach should remain mildly to moderately distended to help remove toxin trapped in rugal folds. If in doubt that the tube has passed down the oesophagus, ideally visualize the pharynx with a laryngoscope or palpate the neck for the presence of the tube in the oesophagus.

7 Attach a funnel onto the oral end of the tube. Using gravity fill the stomach with warm water until it is mildly distended on manual palpation. (Do not connect a hose/tap directly onto the orogastric tube, as this can result in intragastric pressures high enough to cause gastric rupture.) Drop the oral end of the tube below the patient and allow fluid to siphon out. If the tube becomes blocked with gastric contents, flush with water to clear. If this is a repeated problem, try to place a larger tube.

8 Repeat filling and emptying of stomach until the egress fluid is clear. Rotate the animal onto the other side and repeat lavage process until stomach contents run clear. Turn the animal back onto the original side and lavage again. Stomach contents often become caught in the gastric tissue folds and repeated turning and filling of the stomach gives more effective decontamination. Gently rocking the distended stomach by lifting it up from the ventral aspect during egress can help swirl heavy grain-based toxins and improve the effectiveness of the lavage.

9 Allow water to exit around the tube(s) during lavage and drain as much water from the stomach as possible at the end of the lavage.

10 When finished, a charcoal +/– sorbitol mixture can be administered via the tube to decrease absorption of remaining toxin and aid elimination. Use a small-bore stomach tube for administration of activated charcoal. Administration of activated charcoal under anaesthesia increases the risk of regurgitation and aspiration during anaesthetic recovery, but this is the most effective method of ensuring adsorption of any toxin that has passed into the small intestine. Metoclopramide (0.2 mg/kg IM) can be given to increase the lower oesophageal sphincter tone.

11 Kink the gastric tube prior to removal to minimize fluid efflux into the oesophagus.

12 Suction or swab the pharynx and oesophagus prior to extubation. During recovery the animal should be monitored continuously until able to protect its airway. In dogs, keep a cuffed endotracheal tube in place until the dog is conscious and can maintain sternal recumbency and lift its head, to minimize aspiration risk. Avoid delayed extubation in cats because of the risk of laryngospasm.

13 If egress is not complete and the stomach remains distended, the tube may be placed too far caudally and can be obstructed by the stomach wall. Pulling the tube out of the mouth a small distance may re-establish egress flow.

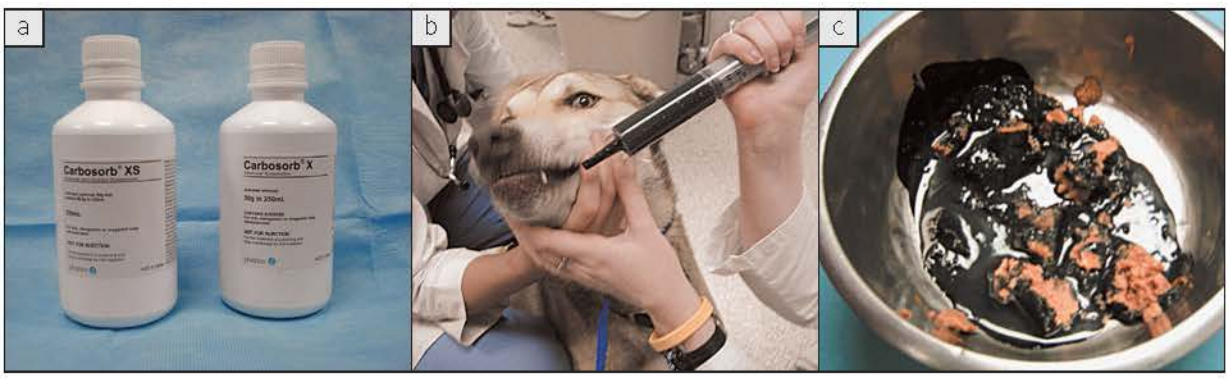
and probably no longer present in the stomach (activated charcoal could be administered instead). A detailed description of gastric lavage is provided in *Table 95*.

Colonic lavage

Colonic lavage is indicated for toxins that may be absorbed from the colon, or in patients who present with clinical signs more than 4–6 hours after ingestion of the toxin. It is generally considered of no benefit if performed within one hour of toxin ingestion except with organophosphates and carbamates, which can track rapidly through the GI tract secondary to the toxins' effects. A narrow non-rigid lubricated tube is advanced from the anus to the level of the transverse colon and warm water is instilled into the colon under gravity flow. (*Note:* Avoid attaching the tube to a mains water tap as this may result in excessive pressure and colonic rupture.) Although this procedure may be performed in obtunded animals, endotracheal intubation is recommended to provide a protected airway, as colonic distension can stimulate emesis.

Activated charcoal

Activated charcoal is indicated for adsorption of most toxins, especially when toxin may still remain in the GI tract or if toxin undergoes enterohepatic recirculation (i.e. excretion of toxins into bile and reabsorption via the intestines). It is contraindicated if the toxin is likely to no longer be present in the GI tract. It is also contraindicated if the patient is judged to have a high risk of charcoal aspiration and the airway cannot be controlled or the patient cannot be closely monitored postadministration. Alcohols, petroleum products, strong acids or alkalis, dissociable salts and metals, such as iron or lithium, are not adsorbed by activated charcoal. The recommended dosage ranges from 1 to 5 g/kg PO. This initial dose may be a charcoal suspension with or without sorbitol (a cathartic) and may be combined with a small amount of food, but additives may decrease the effectiveness of the charcoal (**393**). In toxins with slow GI release and absorption, and in toxins which undergo enterohepatic recirculation, repeated dosing should be performed at a dose of 1–5 g/kg PO every 6–8 hours for 24 hours after exposure. With repeated dosing, the patient must be well hydrated to avoid constipation. The charcoal preparation containing sorbitol should not be used for repeated dosing. Activated charcoal can be administered by stomach tube after gastric lavage, if indicated, or syringe fed if the animal can swallow safely. Occasionally, dogs will willingly drink the charcoal liquid. The efficacy of activated charcoal is altered by addition of mineral oils or dairy products, but the effect of small amounts of dog food or other additives is unknown. Activated charcoal is available as a suspension (with or without sorbitol as an additive) and a powdered form, which must be made into a suspension for administration.



▲ **393** Activated charcoal is available with or without sorbitol as an additive (a). It may be administered directly via dosing syringe (b) or mixed with a small amount of food if the animal will eat the food and charcoal together (c).

Cathartics

Cathartics are used to hasten bowel evacuation and reduce intestinal transit time, in order to minimize the amount of toxin absorbed. They have no benefit in intoxications when administered as sole therapy and activated charcoal should be administered as well. Carthartics are contraindicated in cases of ingestion of caustic materials or in patients with hypovolaemia, dehydration or electrolyte disorders. (See *Table 96* for details on the use of cathartics.)

Additional strategies to decrease toxin levels

Lipid infusions

A recent report in the veterinary literature described the use of intravenous administration of a commercially available lipid solution to assist in the recovery of a patient with severe avermectin toxicity. The infused lipid was postulated to act as a sink for lipophilic drugs, preventing further tissue absorption as well as decreasing tissue levels. The infusions are well described in the human literature for therapy of bupivacaine overdose and may have use for other lipophilic toxicants seen in veterinary medicine. In the single veterinary case report, 20% soybean oil in water (Intralipid®) (**394**) was administered as an intravenous bolus of 2 ml/kg, followed by a CRI of 4 ml/kg/hour for 4 hours. The dose may be repeated in 6–8 hours if clinical signs are still present and the serum is not lipaemic. The dog in the case report received a second dose of 0.5 ml/kg/minute for 30 minutes, 15 hours after the initial infusion. Even though propofol is formulated in a lipid emulsion, it is unlikely to provide a significant lipid sink without significant systemic effects.

Ion trapping

The concept of ion trapping involves purposeful acidification or alkalinization of the urine with the purpose of trapping the ionized form of the toxin in the urine and encouraging excretion. The clinician is encouraged to assess the possible adverse effects of systemic pH modulation on the patient and the severity of intoxication prior to pursuing this route.

Haemodialysis

Haemodialysis uses an artificial circuit to pass the systemic blood through either a filter or adsorbent membrane that can act to remove certain toxicants from the blood quickly and effectively. If haemodialysis is readily available, it may be an appropriate therapy for treating an intoxicated animal.

Table 96 Cathartic solutions

- **Sorbitol 70%**
  - 0.7–1.4 g/kg (1–2 ml/kg) PO once
  - Repeated dosages risk severe osmotic diarrhoea and hypernatraemia
  - Can also be administered by orogastric tube following gastric lavage
  - Usually available in a solution with activated charcoal suspension (the dose is based on the charcoal content)
- **Sodium sulphate (Glauber's salts) 40% solution**
  - 0.25 g/kg PO once, to a maximum of 5 g in cats and 25 g in dogs
  - Repeated dosages risk severe osmotic diarrhoea and hypernatraemia
  - Contraindicated in patients who cannot tolerate elevations in serum sodium (e.g. those with heart or renal disease)



▲ **394** **Intravenous lipid may be administered to patients using regular intravenous infusion pumps.**

SPECIFIC NEUROTOXINS

Neurotoxins can be broadly categorized into neuroexcitatory and neuroinhibitory according to the predominant neurological signs present (*Table 97*):

- Neuroexcitatory toxins affect the CNS, causing hyperexcitability and seizures, and/or affect the peripheral nervous system causing muscle tremors and fasciculations. Ataxia may also occur. Possible systemic complications associated with neuroexcitatory toxins can also include heat stroke (and subsequent complications such as DIC [**395**]), rhabdomyolysis, aspiration pneumonia and secondary neurological injury.
- Neuroinhibitory toxins either affect the CNS, causing obtundation, stupor and coma, and/or affect the peripheral nervous system causing weakness or flaccid paralysis, which, at its most severe, includes respiratory paralysis.

Neuroexcitatory toxins

Bromethalin

Overview

Bromethalin is a rodenticide that was developed for use against warfarin-resistant rats and mice.



▲ **395** **This dog is suffering from disseminated intravascular coagulation secondary to heat stroke. Note the presence of petechiae on the skin in the inguinal region.**

Mechanism of action

Bromethalin leads to uncoupling of oxidative phosphorylation and a subsequent decrease in ATP production in the cell. Inhibition of ATP production leads to dysfunction of the Na^+/K^+ ATP-ase pump within the CNS and an increase in intracellular sodium concentrations. Water then moves into the cells and results in cerebral oedema, increased volume of CSF and vacuolization of myelin. This may result in increased ICP, axonal damage and ultimately inhibition of neural transmission.

The LD_{50} is 4.7 mg/kg in dogs and 1.5 mg/kg in cats. Standard packages contain between 15 and 45 g of 0.01% bromethalin.

Table 97 Differential diagnosis of neuroexcitatory and neuroinhibitory toxins

NEUROEXCITATORY TOXINS	NEUROINHIBITORY TOXINS
Amphetamines	Aminoglycoside overdose
Avermectin	Amitraz
Bromethalin	Avermectin
Brunfelsia	Botulism
Bufotoxins (toad toxicity)	Bromethalin
Carbamates	Coral snake/elapid envenomation
Cocaine	Ethylene glycol
Diethyltoluamide (DEET)	Ivermectin
Ethylene glycol	Latrodectism (black widow/red-back spider envenomation)
Ivermectin	Macadamia nuts
Latrodectism (black widow/red-back spider envenomation)	Marijuana
Lead	Metronidazole
Marijuana	Nicotine
Metaldehyde	Organophosphates (chronic toxicity)
Methylxanthines	Tetrodotoxins
Mycotoxins (tremorgenic)	Tick paralysis
Nicotine	Tricylcic antidepressents
Organochlorines	
Organophosphates	
Permethrin	
Phencyclidine (PCP)	
Pseudoephedrine	
Salt (sodium chloride)	
Sodium monofluoroacetate (1080; SMFA)	
Salicylates (overdose)	
Strychnine	
Tricyclic antidepressants	
Zinc phosphide	

Non-toxic causes should also be considered as differential diagnoses

Clinical presentation

Higher doses produce acute signs of hyperexcitability, hyperaesthesia, muscle tremors, focal or generalized seizures and hyperthermia within 2–24 hours of ingestion. Low to moderate doses produce the more common clinical presentation of hindlimb ataxia, extensor rigidity, decreased conscious proprioception and paresis that can progress to paralysis. CNS depression is also usually present, with more severely affected animals becoming comatose. These signs may not manifest until 1–3 days after exposure. In the later/terminal stages, animals may develop seizures and a decerebrate posture. Cats may experience a slower onset and longer duration of clinical signs than dogs.

Diagnosis

Antemortem diagnostics are not available. Bromethalin or its metabolites can be detected in the liver, kidney and brain. Samples should be submitted frozen and protected from light.

Management

No antidote is available. Decontamination is by induction of emesis. Alternatively, gastric lavage should be performed to remove any bromethalin within the stomach. Repeated doses of activated charcoal (1–5 g/kg q6–8h) should be administered for at least 48 hours after ingestion to decrease absorption and reduce enterohepatic recirculation of the bromethalin and its metabolites. Use of a cathartic (sorbitol) is recommended with the initial dose of activated charcoal.

Excessive muscle tremors can be controlled using methocarbamol (initial dose 44–220 mg/kg IV, given in small boluses of 30–40 mg/kg until tremors have improved or ceased). Methocarbamol is a centrally-acting muscle relaxant. It is stated to have a maximum 24-hour dose of 330 mg/kg for cats and dogs. If injectable methocarbamol is unavailable, it may be administered orally or the tablets may be ground up, dissolved in water and administered per rectum at the same doses used for intravenous administration. Diazepam (0.5 mg/kg IV) can be used for seizures and mannitol (0.5–1.0 g/kg IV) or 7% hypertonic saline (1–3 ml/kg IV) to help reduce cerebral oedema.

Supportive care should focus on maintaining normal cardiovascular parameters (heart rate and BP) in an effort to maximize CPP. Care should be taken to avoid hyperthermia and hypercapnea. Bladder management, nutrition supplementation and general nursing care should be instituted in paretic patients. The use of corticosteroids has previously been suggested for bromethalin toxicosis; however, there is no evidence to support this recommendation and thus their use is not indicated.

Prognosis

The prognosis is guarded to grave due to the severity of clinical signs seen at even low doses of exposure, as well as the lack of an antidote. Animals with mild clinical signs can recover and full resolution of clinical signs may take several weeks; however, some will have permanent neurological dysfunction.

Brunfelsia spp.

Overview

Brunfelsia spp. (also known as yesterday, today and tomorrow) (**396**) is related to other plants, such as the Carolina jasmine (*Gelsemium sempervirens*), and exposure to either causes similar clinical signs. It is found in coastal regions of the USA and Australia. Semi-shade conditions in rich acid soil with a generous water supply appear best for plant growth.

Mechanism of action

All species and all parts of the plant (flowers, leaves, berries and seeds) are considered toxic to dogs. There are no reports of toxicity in cats. The toxic principle is thought to be brunfelsamidine; however, multiple biologically active compounds have been isolated. The toxic component is water soluble and stable for up to 4 months.

Clinical presentation

The GI tract and CNS are most commonly affected, with signs occurring within a few hours of ingestion. GI signs precede neurological signs and include vomiting, hypersalivation and diarrhoea. CNS signs initially include agitation, nervousness or excitement, followed by tremors, shaking, paddling and tonic–clonic seizures. Later signs closely resemble those of strychnine poisoning. Muscle rigidity in animals can result in a 'sawhorse' stance. Symptoms may resolve within a few hours or last for several days, despite therapeutic intervention.



▲ 396 The flowers and leaves of *Brunfelsia* spp. (also called 'yesterday, today and tomorrow' due to its colour variation). (© Mary Pinké Neck, used with permission.)



▲ 397 Cane toad (*Bufo marinus*). (© Simon Lemin, used with permission.)

Diagnosis

Diagnosis is generally presumptive based on a history of ingestion or exposure to the plant. The presence of seeds, seed pods or berries in the vomitus or stool can help to confirm suspicions.

Management

Induction of emesis or gastric lavage should be considered if the toxicity is recent and especially if large amounts of seeds or berries have been ingested. Activated charcoal is recommended every 4–6 hours after emesis for 24 hours or until resolution of clinical signs. A cathartic can be given with the first dose of activated charcoal, but should not be used in patients who already have diarrhoea. Intravenous fluid administration for 1–2 days after ingestion may be required to help promote excretion and maintain hydration during recovery.

Seizures may be treated with benzodiazepines or barbiturates, although variable success in control of seizures due to *Brunfelsia* toxicity has been noted with diazepam. Severely affected animals may require anaesthesia, intubation and mechanical ventilation. Methocarbamol may be used for muscle relaxation. Animals should be kept in a quiet, dimly lit area to decrease exacerbations of nervousness or excitement.

Prognosis

Complete recovery may take several days or weeks.

Bufotoxins (toad toxicity)

Overview

There are over 200 species of *Bufo* toads throughout the world. One of the most common toads associated with intoxications around the world is *Bufo marinus* (cane toad) (**397**). In the USA, this toad is found mainly in Florida, and it is found in the north and northeast of Australia. This section is specific to toxicity from *Bufo marinus* except where otherwise specified. Toad toxicity occurs most commonly during periods of high rainfall or high temperatures and in the evenings when toads are active.

Mechanism of action

The severity of toxicity is determined by the dose received and the patient's body size, therefore small dogs that mouth large toads tend to be more severely affected. In endemic regions, canine intoxication is common; cats are rarely affected. Toxicity most commonly occurs in young small breeds of dogs, with Terriers overrepresented. Some dogs will require repeated treatment secondary to toad-catching behaviour.

Toxins are produced in large volumes in the parotoid glands on the dorsum of the toad as well as in other glands found throughout the skin of the toad. Dogs may compress the parotoid glands when biting toads, thereby releasing venom into their mouth; alternatively, toads may also squirt venom towards other animals. Venom is tenacious and sticks to mucous membranes. Toad toxins are rapidly absorbed across oral mucous membranes, conjunctiva, gastric mucosa and open wounds.

Components of toad venom include bufotenines, bufogenins (bufadienolides), bufotoxin and catecholamines. Bufotenines have hallucinogenic effects due to serotonin and 5-hydroxytryptophan. Bufogenins and bufotoxins have effects similar to those of digitalis (cardiac glycosides) and inhibit Na^+/K^+ adenosine triphosphate enzymes, resulting in bradyarrhythmias and supraventricular or ventricular tachyarrhythmias. Bufotoxins also have vasoconstrictive effects. Catecholamines,which include epinephrine, norepinephrine and dopamine, cause tachycardia, hypertension and seizures.

Complications can include cerebral oedema secondary to prolonged seizure activity, heat stroke and cardiac arrest.

Clinical presentation

Clinical signs occur within minutes to 1 hour after exposure. The most common clinical signs include salivation, brick-red mucous membranes, pawing at the mouth, altered mentation, vomiting, extensor rigidity, nystagmus and seizures. Other signs include weakness, ataxia, cardiac arrhythmias, muscle tremors, tachypnoea, anisocoria, mydriasis, opisthotonus and pulmonary oedema. Sinus arrhythmia and sinus tachycardia are the most common ECG rhythms reported; however, sinus bradycardia and first- and second-degree heart block occur less commonly.

In the UK, *Bufo vulgaris* causes severe oral inflammation, profuse salivation, retching and vomiting for up to 12 hours when mouthed by animals. Systemic signs have only been reported in cats and take longer than 24 hours to occur; these include abdominal pain, ataxia and temporary blindness. Recovery may take up to 6 days.

Diagnosis

Diagnosis is based on confirmed contact with a toad and appropriate clinical signs. Blood digoxin levels may be elevated.

Management

Decontamination is performed by copious washing of the animal's mouth to remove the secretions. Ocular lavage may also be required. In the rare situation where the toad has been ingested, emesis, gastric lavage or endoscopic removal may be required. Owners should not be advised to hose their dog's mouth as this has been associated with pulmonary aspiration of the water. Instead, they should be advised to wipe secretions out of the mouth with a wet cloth.

Intravenous fluids should be given to patients with significant cardiac effects, as bufogenins are excreted in the urine. Diazepam should be administered to control any seizures; if this is ineffective, the use of pentobarbital or propofol is indicated. Phenobarbital can also be administered for sedation or seizure control. Antiarrhythmic drug therapy should only be instituted if the arrhythmias are associated with decreased cardiac output. ECG analysis is required to decide on appropriate drug therapy, as bradycardias as well as tachycardias may occur. Lidocaine, propranolol and verapamil have all been shown to decrease the incidence of ventricular fibrillation secondary to toad toxin-induced ventricular arrhythmias. Esmolol is another potential treatment. Propranolol may predispose to significant bradycardia in anaesthetized patients.

Atropine should be avoided unless bradycardia is associated with decreased cardiac output. Because of the potential for atropine-induced sinus tachycardia it should not be used to control salivation. Digoxin-specific Fab fragments have been used in humans suffering significant cardiac effects secondary to ingestion or inhalation of toad herbal products. Digoxin-specific Fab fragments are antibody fragments produced by immunizing sheep with a digoxin derivative.

Supportive care should also be instituted.

Prognosis

Up to 96% survival rates have been reported with appropriate decontamination and supportive care. Small animals are more likely to be hospitalized, whereas large dogs may only require oral decontamination before discharge.

Ivermectin and other macrolide parasiticides

Overview

This drug class, also known as avermectins or macrocyclic lactones, includes ivermectin, moxidectin, selamectin, milbemycin, doramectin, eprinomectin and abamectin. Toxicity may occur secondary to ingestion of large-animal deworming products or contaminated faeces. Overdose may be iatrogenic if owners inappropriately administer topical products orally or give inappropriate doses of anti-parasitic medications. A high percentage of Collies and related herding breeds of dog have an increased genetic susceptibility for toxicity due to ineffective blood–brain barrier efflux pumps.

Mechanism of action

Macrolide antiparasitic drugs cause toxicity in mammals by acting as agonists at the $GABA_A$-gated chloride channels in the CNS. Initially, this may result in neuroexcitation, but at higher doses can result in flaccid paralysis and coma. Collies, Border Collies, Shetland Sheepdogs, Australian Shepherd Dogs and herding breeds of dogs have a high incidence of a mutation in p-glycoprotein (MDR1), which serves as an efflux pump for lipophilic compounds in the CNS. This results in increased accumulation of the drug within the CNS and clinical signs of neurotoxicity at doses safe for dogs without this mutation. Occasionally, dogs from breeds not previously reported to have increased susceptibility to avermectins may develop signs of toxicity at low doses.

Toxicity in dogs is unlikely to occur at prophylactic heartworm doses of ivermectin (6 mcg/kg), even in susceptible breeds. Ivermectin toxicity in susceptible dogs may occur at doses as low as 0.1 mg/kg, whereas non-susceptible breeds may not develop toxicity until doses of 2.5 mg/kg are exceeded. The LD_{50} for Beagles has been reported to be 80 mg/kg. Cats may be more sensitive to ivermectin and 0.3–1.3 mg/kg subcutaneously may be enough to cause signs of toxicity. Many of these drugs have long half-lives for elimination; in dogs this ranges from 2 days for ivermectin to 19 days for moxidectin. Enterohepatic recirculation does occur.

Diagnosis

Diagnosis is based on a history of exposure or iatrogenic administration of macrolide drugs. Testing for MDR1 genotype can be carried out to assess for defective p-glycoprotein in dogs who appear to have increased susceptibility. These animals will probably have increased sensitivity to other drugs such as opioids. Some laboratories will assay blood levels of macrolides.

Clinical presentation

Signs of toxicity in dogs and cats include ataxia, lethargy, tremors, mydriasis, blindness, hypersalivation, disorientation and seizures. This may progress to weakness, stupor, coma and respiratory failure.

Management

In cases of recent ingestion, emesis may be induced as long as the animal is alert. If the animal is stuporous or comatose and a large amount of drug has been ingested, gastric lavage may be considered. Repeated doses of activated charcoal (1–5 g/kg every 6–8 hours for 6 treatments) can be given. The use of intravenous lipid infusion may limit the duration or severity of clinical signs.

Seizure control is achieved primarily using barbiturate drugs such as phenobarbital. Historically, benzodiazepines were thought to exacerbate clinical signs of avermectin toxicoses due to proximity of binding sites on the GABA receptor, and so were not recommended as first-line seizure control. It has been recently postulated that this may not be the case. If sedation or prolonged anaesthesia is required, a propofol CRI is a better option than repeated benzodiazepine administration.

Supportive care, which in severe cases may necessitate ventilatory support, should be given.

Prognosis

The prognosis is guarded if the ivermectin dose received is >5 mg/kg. Recovery may be prolonged, especially in animals exposed to a longer-acting drug such as moxidectin, taking 2–3 weeks for full recovery.

Lead

Overview

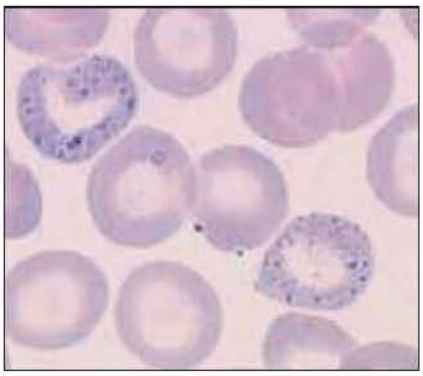
Sources of lead can include lead-based paint (products made prior to 1977), batteries, plumbing materials, lead sinkers, bullets or pellets, lead foil, lubricants (grease or used motor oil), toys, golf balls or roofing materials. Owners of pets with suspected lead toxicity should be advised to evaluate the environment, especially if small children are present, as animals may manifest clinical signs prior to people who share the same environment.

Mechanism of action

Lead binds to sulfhydryl groups and interferes with many sulfhydryl-containing enzymes, resulting in interference of haem synthesis, increased RBC fragility and basophilic stippling (**398**). Neurotoxic mechanisms are unclear, but postulated effects of lead on the CNS include interference with the action of GABA, capillary damage resulting in cerebral haemorrhage and neuronal necrosis, competitive inhibition of calcium and interference with dopamine uptake.

Clinical presentation

Vomiting, anorexia, abdominal pain and occasionally diarrhoea are the initial signs of intoxication. Other clinical signs may include lethargy, polyuria, polydipsia, weight loss, pica or aggression. Neurological manifestations include behaviour changes, ataxia, head pressing, blindness, tremors, polyneuropathy and seizures. Signs can be intermittent, with periods of normal behaviour. Clinical signs may vary based on duration of exposure, amount ingested, the form of lead ingested and the age of the patient (younger animals are more commonly affected).



▲ **398** Red blood cells in this blood smear display basophilic stippling characteristic of lead toxicity.

Diagnosis

In illness caused by chronic exposure, historical findings are not always reliable; however, a history of recent home renovation and possible exposure to, or ingestion of, lead-containing paint may be relevant. The presence of high numbers of nucleated RBCs and basophilic stippling (especially in dogs, **398**) can be found in cases of lead intoxication. Mild anaemia may be seen in chronic lead poisoning, but generally is not present in acute cases.

Radiographs may be useful in identifying the presence of metallic foreign objects either within the GI tract or subcutaneous tissue. Confirmation of poisoning can be made by analysis of whole blood lead levels. Samples may be anticoagulated with heparin or EDTA; however, contact with the laboratory should be made to determine the preferred anticoagulant, since certain methodologies will be inaccurate with EDTA samples. Clinical signs combined with blood levels that exceed 0.35 ppm or urine levels that are >0.75 ppm are consistent with acute intoxication.

Management

Emesis should be induced to remove any lead product present in the stomach. Endoscopic retrieval or surgical removal, particularly for bullets or fragments present in subcutaneous tissue, may be necessary. Magnesium sulphate (250–500 mg/kg PO for dogs; 200 mg/kg PO for cats) can be used as a cathartic and to reduce absorption by forming insoluble lead sulphate.

Chelation therapy is aimed at removing lead from the blood and soft tissues. Succimer (meso-2,3-dimercaptosuccinic acid) (10 mg/kg PO q8h for 10 days) is the preferred chelating agent. Succimer can be given rectally in animals who are vomiting or in those unable to take oral medication (i.e. seizuring or obtunded patients). It has a wide margin of safety; however, side-effects may include GI upset or a rebound in blood lead levels after treatment, which may necessitate an additional 10-day course.

Calcium EDTA (27 mg/kg SC q6h for 5 days) has commonly been used in dogs and cats to chelate lead. Injections should be diluted in saline to a final concentration of 10 mg/ml (or less) to help reduce pain associated with the injection. Renal tubular necrosis may result from administration of calcium EDTA and thus it should be avoided in patients with diminished renal function and limited to a maximum of 5 consecutive days. It may be repeated in 2–3 weeks if blood lead concentrations remain elevated. It may also be administered slowly intravenously (5 mg/kg/day divided q12h); however, this should be used with caution as increases in ICP have occurred in people with cerebral oedema after intravenous administration.

D-penicillamine (33–55 mg/kg/day divided q6–8h) may be used as an alternative to, or in conjunction with, calcium EDTA. Dosages up to 110 mg/kg/day have been used; however, GI side-effects usually limit use to the lower dosage. Administration for 1 week, followed by discontinuation for 1 week and a subsequent week of therapy, has also been recommended.

Seizure activity should be treated with benzodiazepines. Since cerebral oedema may contribute to seizures in cases of severe intoxication, mannitol (0.5–1 g/kg IV given over 20 minutes) should be used in cases with severe or prolonged seizures.

Thiamine supplementation (1–2 mg/kg IM or 2 mg/kg PO q24h) has resulted in improvement in neurological signs associated with lead toxicosis in some animals. Zinc supplementation (especially in patients receiving calcium EDTA) can help prevent chelation-induced zinc deficiency.

Prognosis

Response to treatment is one of the best indicators of prognosis, and is generally favourable for animals that undergo chelation therapy. Continuous or uncontrolled seizures may warrant a poorer prognosis and can result in permanent neurological deficits.

Metaldehyde

Overview

Metaldehyde is found in slug and snail baits and it is also used as a camping fuel. Large volume ingestion of snail and slug pellets is common, as dogs are attracted to the bran and molasses included in the pellet.

Mechanism of action

Metaldehyde decreases levels of the inhibitory neurotransmitter GABA, while increasing monoamine oxidase activity and decreasing levels of noradrenaline and serotonin (5-hydroxytryptamine, 5-HT). Both aspects can have a pro-convulsive effect. The LD_{50} starts at 100 mg/kg PO in dogs and 207 mg/kg PO in cats. Heat stroke and its associated complications are common in metaldehyde toxicity.

Clinical presentation

Clinical signs develop rapidly after ingestion. Anxiety, muscle tremors, muscle fasciculations, ataxia and then seizures appear in a progressive order. Tachypnoea, hyperthermia and tachycardia are also often seen. Diarrhoea is rare unless the affected dog develops heat stroke. Metabolic acidosis is common. Severe cases will present in lateral recumbency, comatose and with generalized muscle rigidity.

Diagnosis

Diagnosis is based on a history of witnessed ingestion or recent garden treatment with metaldehyde pellets, combined with appropriate clinical signs. Bait may be found in gastric contents, which should be frozen for laboratory analysis if required.

Management

Emesis should be induced for acute ingestion (≤3 hours) and only in those at minimal risk for aspiration (mildly affected, able to stand and walk with minimal ataxia). If patients are recumbent or have severe ataxia, GA for gastric lavage is indicated. Gastric lavage can be productive more than 3 hours after ingestion if a large volume of bait has been consumed. Activated charcoal is effective and should also be administered to prevent further absorption.

Muscle tremors can be managed with methocarbamol. Generalized seizures are initially managed with short-acting injectable drugs such as benzodiazepines or phenobarbital, but may need prolonged therapy in the form of long-acting anticonvulsants or intravenous infusions of an anaesthetic such as propofol. GA using inhalant anaesthetics has also been reported to control intractable seizures in metaldehyde-poisoned canine patients.

With effective GI decontamination and limited clinical signs, prolonged anaesthesia is generally not required. If >4–6 hours of anaesthesia is required to control seizures, then either inadequate GI decontamination or another cause of seizures should be suspected. Supportive care is required for heat stroke and metabolic acidosis. Inadequate clearance of toxin from the stomach may be secondary to decreased gastric motility caused by the metaldehyde.

Prognosis

The prognosis is generally good if aggressive and rapid supportive care and GI decontamination are instituted early and heat stroke has not developed. Reported mortality rates for dogs with metaldehyde toxicoses range from 0% to 17%. The prognosis is guarded for patients who present with temperatures >41.6°C (106.9°F) or who have developed hypoglycaemia or complications associated with heat stroke, such as DIC.

Methylxanthines

Overview

This class includes caffeine, theobromine (found in chocolate) and theophylline.

Mechanism of action

Methylxanthines are phosphodiesterase inhibitors that cause an elevation in intracellular cyclic AMP (cAMP). Increased cAMP results in increased intracellular calcium, causing NM excitability as well as a positive inotropic effect. Competitive inhibition of adenosine receptors also results in CNS stimulation, as well as further increases in intracellular cAMP, which may additionally contribute to the development of cardiac arrhythmias. For caffeine and theobromine the LD_{50} is 100–200 mg/kg. Animals ingesting 20 mg/kg may have mild clinical signs and seizures may occur at 60 mg/kg. The theobromine content of specific sources is listed in *Table 98*. The lethal toxicity for theophylline is reported to be 300 mg/kg PO in dogs and 700 mg/kg PO in cats.

Table 98 Estimated theobromine levels in chocolate products

- Milk chocolate: 1.6–2.3 mg/gram (45–65 mg/oz)
- Semi-sweet chocolate: 5.3 mg/gram (150 mg/oz)
- Dark chocolate: 10.6 mg/gram (300 mg/oz)
- Baker's (unsweetened) chocolate: 14.1–15.8 mg/gram (400–450 mg/oz)
- Cocoa bean mulch: 10.6 mg/gram (300 mg/oz)
- Cocoa beans: 10.6–42.3 mg/gram (300–1,200 mg/oz)
- White chocolate: negligible content

Clinical presentation

Clinical signs generally occur within 1–2 hours post ingestion and initially include restlessness, hyperactivity and mild hyperreflexia. Vomiting and diarrhoea are also among some of the first signs seen, especially if chocolate is the source. At higher doses, severe tachycardia (200–300 bpm), tachypnoea, polyuria, hyperactivity, muscle twitching and tonic to tetanic convulsive seizures are seen. Hyperthermia is also often seen. Clinical signs generally last for 12–24 hours, but can persist for up to 72 hours.

Diagnosis

A history of chocolate ingestion or of vomitus with chocolate is frequently seen and suggestive of toxicity when accompanied by appropriate clinical signs. Stomach contents, serum, plasma or urine can be analysed for methylxanthine levels. Theobromine may be detected in serum 3–4 days after the initial ingestion. Levels are stable in plasma or serum for up to 7 days at room temperature and 14 days if refrigerated.

Management

Emesis should be induced in patients with known or suspected exposure 2–4 hours prior to presentation. Activated charcoal every 3–4 hours may help to reduce further absorption and increase excretion. The use of activated charcoal containing a cathartic (sorbitol) is recommended for the first dose only.

Intravenous fluid therapy can be beneficial in increasing urinary excretion of methylxanthines, as well as maintaining cardiovascular stability. Placement of a urinary catheter will help to prevent reabsorption of metabolites across the bladder mucosa.

Ventricular arrhythmias compromising cardiac function should be treated with lidocaine in dogs. An initial bolus of 1–2 mg/kg IV should be given, followed by an infusion of 30–75 mcg/kg/minute IV. In cats, a lower bolus dose of 0.25–0.5 mg/kg IV and an infusion of 10–20 mcg/kg/minute IV is recommended. Cats are susceptible to CNS toxicity secondary to lidocaine. Additional medications, such as procainamide (6–10 mg/kg IV slowly over 10–15 minutes) or calcium channel blockers (e.g. diltiazem, 0.1–0.2 mg/kg IV), may be beneficial in cases of severe arrhythmias. Beta-blockers may be needed for persistent tachycardias; however, propranolol reportedly delays renal excretion of methylxanthines, so esmolol may be more appropriate. Patients should be monitored carefully for hypotension and cardiac rhythm while administering antiarrhythmic therapy.

Muscle tremors can be managed with methocarbamol. Seizures generally are controlled with benzodiazepines; however, additional use of barbiturates or anaesthetics may be indicated for severe cases. Hyperthermic animals should be cooled appropriately.

Prognosis

The prognosis is generally good for animals that are treated early and aggressively or who have mild to moderate clinical signs. Animals that develop severe seizures or arrhythmias may have a more guarded prognosis. Animals that have ingested large amounts of milk chocolate may develop pancreatitis due to the high fat content of the chocolate; it is prudent to alert owners to this possible sequela.

Mycotoxins (tremorgenic)

Overview

The most common tremorgenic mycotoxins are penitrem A (produced by *Penicillium crustosum*) and roquefortine (produced by *Penicillium roquefortine* and other *Penicillium* species). Other less common tremorgenic mycotoxins have been reported. Mouldy foods (nuts, garbage, soft cheeses) and compost may all be sources. Penitrem A is most likely to be produced in food materials that have a high moisture content.

Mechanism of action

The actual mechanism of toxicity is unknown, but is thought to be related to the inhibitory actions of glycine in the CNS. It is possible that the toxin inhibits glycine release or antagonizes the actions of glycine in inhibitory neurons. There is also a possibility that some mycotoxins result in increased pre-synaptic neurotransmitter release. In one small study of intraperitoneal toxicity of penitrem A in dogs, doses from 0.125 mg/kg resulted in tremors and doses of 0.5 mg/kg to 5 mg/kg also resulted in intermittent periods of seizure activity and finally death in the majority of untreated dogs. Seizure length and severity appeared to worsen with higher doses.

Both penitrem A and roquefortine are rapidly absorbed after oral ingestion. They are excreted via bile and enterohepatic recirculation may occur.

Clinical presentation

The onset of clinical signs can occur 30 minutes to several hours postingestion. Signs include hyperaesthesia, anxiety, restlessness, panting, vomiting, salivation, mild to severe muscle tremors and fasciculations, seizures and SE. There is a potential for hyperthermia, heat stroke and rhabdomyolysis secondary to the tremors.

Diagnosis

Diagnosis is based on a history or suspicion of ingestion of mouldy food. Penitrem A or roquefortine can be identified in vomitus or food material via mass spectrometry, thin layer chromatography or quantitative analysis via high-pressure liquid chromatography. If toxin identification is unavailable, then culture of food or vomitus and growth of *Penicillium* or other mycotoxin-producing fungus is compatible.

Management

Emesis or gastric lavage should be induced if there is recent or large volume ingestion. Activated charcoal should be administered q6h for 24 hours due to enterohepatic recirculation of toxins. Benzodiazepines +/- methocarbamol can be used to control tremors and phenobarbital may also be used for tremor/seizure control. In severe cases, GA may be required. Supportive care should be provided as indicated.

Prognosis

The prognosis is generally good with appropriate supportive care and effective GI decontamination. However, the prognosis is guarded if GI decontamination is incomplete in the face of a large dose of ingested mycotoxin. Recovery can be very rapid, but commonly occurs over 24–48 hours and occasionally is prolonged to up to 4–5 days.

Nicotine

Overview

Sources of nicotine include tobacco products, smoking cessation drugs and patches, and insecticides.

Mechanism of action

Low doses of nicotine mimic ACh and result in stimulation of the post synaptic nicotinic receptors. At high doses the initial stimulatory effects are followed by blockade at the NM junction caused by persistent depolarization. Nicotine also directly stimulates the emetic chemoreceptor trigger zone. The LD_{50} in dogs is 9.2 mg/kg.

Clinical presentation

Rapid onset of hyperactivity, vomiting and salivation are generally seen within 1 hour of ingestion. Miosis and repeated defecation have also been reported. Bradycardia can result from vagal stimulation. Tremors and convulsions may also be noted in the early phases of high-dose intoxication. These may progress to depression, weakness, paralysis and death. Hypotension as a result of vasodilation may occur. Death is primarily as a result of respiratory paralysis.

Diagnosis

A detailed history, in combination with clinical signs, may reveal exposure to nicotine. It may be detectable in the stomach contents or urine.

Management

Emesis should be induced if ingestion was within 2 hours of presentation. The administration of activated charcoal every 4–6 hours for 12–24 hours is recommended to prevent absorption. Intravenous fluid therapy is recommended to help increase excretion. Atropine may be necessary in cases in which severe parasympathetic effects are seen. Seizures may be controlled with benzodiazepines or phenobarbital. In cases of hypoventilation from respiratory paralysis, mechanical ventilation should be performed.

Alkalinization of the stomach increases absorption, therefore antacid medications such as H_2-blockers and proton pump inhibitors are contraindicated. The majority of ingested nicotine is eliminated within 16–20 hours.

Prognosis

The prognosis for ingestion of small amounts with mild clinical signs is generally good. Larger intoxications and increased severity of clinical signs generally warrant a poorer prognosis.

Organochlorines

Overview

Organochlorines are potent pesticides that were used more frequently in the 1970s. Exposure from contaminated environments, old dump sites or stored supplies are still occasionally seen.

Mechanism of action

The full mechanism of organochlorine toxicity is incompletely understood. Most organochlorines result in a persistent opening of sodium channels within neurons, resulting in repetitive firing of action potentials and a slower repolarization. Some of the organochlorines are also inhibitors of GABA. Organochlorines are highly lipid soluble. After ingestion, plasma levels peak then quickly decline as the compound redistributes into fat stores. Extensive enterohepatic recirculation can lead to prolonged clinical signs. The LD_{50} for mammals is 50 mg/kg.

Clinical presentation

Initially, hypersensitivity, nervousness, agitation and tremors may be seen. These signs may develop within a few minutes after exposure or can be delayed for up to 2 days. Other signs may include weakness, vomiting or respiratory depression. Advanced signs include a spastic gait, continuous clamping of the jaws, abnormal posture or tonic–clonic seizures. Some animals may be depressed between seizures, while others remain comatose. Seizures may last for up to 48–72 hours. Hyperthermia may be present in patients with prolonged seizure activity.

Diagnosis
Organochlorines can be detected in multiple tissues, including fat, blood, liver or brain. All tissue samples should be submitted in glass or metal containers (avoid plastic containers).

Management
No antidote is available, and treatment is symptomatic and supportive. Emesis should be induced in acute ingestion. Gastric lavage can be useful if a large exposure is suspected. To prevent absorption, activated charcoal should initially be given q4–6h after acute ingestion. Since pesticide residues can persist long term and undergo extensive enterohepatic recirculation, daily dosing of activated charcoal has been recommended for 1–2 weeks after exposure. Benzodiazepines, barbiturates or levetiracetam can be given for seizure control. In severe cases, GA may be required. Severe intoxications resulting in comatose states and respiratory depression may require ventilatory support.

Prognosis
Patients with prolonged seizure activity or who remain comatose have a grave prognosis.

Organophosphates and carbamates
Overview
These toxins are commonly used in agriculture and for domestic garden and household pest use. Additionally, they are used for external parasite control. Pets are generally exposed by ingestion or dermal contact.

Mechanism of action
OPs and carbamates inhibit the action of AChE, allowing ACh to accumulate at cholinergic synapses. Continued stimulation at cholinergic synapses results in excessive stimulation of the distal neuron, gland or muscle, causing (1) familiar cholinergic signs of muscarinic toxicity, which include salivation, lacrimation, urination and defecation, in addition to bronchospasm, (2) CNS toxicity (depression, decreased level of consciousness and seizuring), and (3) nicotinic toxicity (weakness and muscle tremors). OPs bind tightly to AChE and can become permanently bound, which is known as 'ageing' of the AChE. There are three syndromes associated with OP toxicity:

- Acute toxicity.
- Intermediate syndrome for which the underlying pathology has not been determined.
- OP-induced delayed neuropathy (OPIDN), which is a toxin-induced degeneration of the long motor nerves.

Carbamates do not become permanently bound and they bind to AChE for a significantly shorter period, generally <40 minutes.

Clinical presentation
Acute toxicity presents with a combination of muscarinic, nicotinic and CNS signs:

- Muscarinic clinical signs include hypersalivation, lacrimation, urination, defecation, diarrhoea, vomiting, miosis, bradycardia, bronchospasm and bronchorrhoea. Respiratory compromise may result in cyanosis. Tachycardia and mydriasis may be present secondary to catecholamine release.
- Nicotinic clinical signs include muscle fasciculations, muscle twitches and tremors. Weakness and paralysis can be a delayed NM sign.
- Central nervous system signs include anxiety, ataxia, seizures, obtundation and coma.

The intermediate syndrome develops 7–96 hours after an acute OP toxicity. Clinical signs of severe NM weakness are present, particularly affecting the cranial half of the body, with cervical ventroflexion, forelimb weakness and hypoventilation reported.

Chronic toxicity or exposure can cause OPIDN. This generally occurs 1–4 weeks after exposure to the OP. Anorexia, lethargy, hindlimb paresis, hyperaesthesia and cervical ventroflexion have been reported in cats. Anorexia is an early sign.

Diagnosis
Known contact with the toxin and appropriate clinical signs are compatible with the diagnosis. Whole blood cholinesterase activity <25% of normal can be diagnostic. Values <50% of normal are suspicious in both acute toxicity and the intermediate syndrome. Reference levels, which are normally measured on heparinized whole blood, are specific to the laboratory. Sample handling and transport should be confirmed with the laboratory.

Cholinesterase activity testing can be problematic in carbamate toxicity due to the short half-life of carbamate's binding to cholinesterase; the cholinesterase activity may normalize during transport. Gastric contents can be tested for the specific toxin in acute ingestions. An atropine response test can be used in suspected cases of acute OP or carbamate toxicity: 0.02 mg/kg atropine is given intravenously; if muscarinic signs resolve and mydriasis and tachycardia develop, then acute OP or carbamate toxicity is not present and no further atropine should be administered.

Management

Acute toxicity

If there is dermal exposure, decontamination is by washing. If the exposure is oral, decontamination is by emesis, lavage and activated charcoal.

Atropine is the antidote for muscarinic signs; it has no effect on nicotinic and central signs. If severe or life-threatening muscarinic signs (cyanosis, bradycardia, bronchial secretions) are present, the use of atropine is indicated. An initial dose of 0.02 mg/kg IV can be administered as an atropine response test if there is any uncertainty about the diagnosis. Rapid resolution of muscarinic signs at this dose of atropine indicates that OP or carbamate toxicity is unlikely. Atropine doses of up to 0.1–0.5 mg/kg can be administered slowly (1/4 slow IV; remainder IM if required) to effect in confirmed cases until cyanosis, dyspnoea, salivation and bradycardia are resolved. For carbamate toxicity lower doses are generally required because of the short half-life of carbamate toxicity and repeated doses of atropine are unlikely to be required. With OP toxicity, higher and repeated doses are frequently required. Atropine frequently causes gut stasis (delaying GI transit times) and this should be taken into account when treating orally ingested OPs and carbamates with minimal muscarinic signs.

Pralidoxime (2-PAM) (10–20 mg/kg SC, IM or slow IV up to q8h) acts to reactivate phosphorylated cholinesterase and is indicated for severe nicotinic signs of OP toxicity. Atropine should be co-administered with 2-PAM. 2-PAM has anticholinesterase properties and can cause clinical signs of OP toxicity if used when OP toxicity is not present or when the OP has become permanently bound to AchE and can no longer be dislodged by the 2-PAM. In carbamate toxicity there is a risk that administration of 2-PAM may worsen clinical signs, which is definitely the case with carbaryl toxicity. Diazepam can be administered for seizures.

Intermediate syndrome

Supportive care, including ventilation when required, should be administered. 2-PAM may be useful if given before permanent 'ageing' of AChE occurs; however, there have been anecdotal reports of death of cats in association with use of this drug.

Organophosphate-induced delayed neuropathy

OPIDN treatment involves removal of the source of the OP and supportive care. Diazepam should not be used as an appetite stimulant in cats suffering from chronic toxicity as it has occasionally been associated with the development of muscle tremors and muscarinic signs. The mechanism for this is unknown.

Prognosis

The prognosis for acute toxicity is good if the patient survives the initial toxicity. Potential complications include aspiration pneumonia, intussusceptions and the side-effects of heat stroke if severe hyperthermia develops. The prognosis for the intermediate syndrome and OPIDN appears to be good if appropriate supportive care is provided, but weeks of support may be required for OPIDN and ventilation may be required for severe cases of intermediate syndrome.

Permethrin

Overview

Permethrin is a lipid-soluble synthetic pyrethroid, a class of compound originally derived from chrysanthemum. This is a common toxicity in cats, generally resulting from inappropriate topical administration of specific 'spot-on' flea products or rinses by owners. Secondary exposure may occur in cats that are in close contact with treated dogs or environments. Pyrethroids can also be found in medicated shampoos, some flea collars and environmental insecticidal treatments. Significant exposure in cats may also occur due to oral ingestion by grooming behaviour. Cats have reportedly been exposed by licking empty packets of spot-on products. Other synthetic pyrethroids cause similar clinical effects.

Mechanism of action

Pyrethroids can slow both opening and closure of voltage sensitive sodium channels, interfering with depolarization of nerves and resulting in repetitive nerve discharges or prolonged depolarization. Motor and sensory nerve fibres are affected and the lipophilic character of the compounds encourages accumulation and persistence in neural tissues.

Cats may have increased susceptibility due to deficiencies in hepatic glucuronidation, which slows initial detoxification of these compounds. The minimal toxic dose is unknown; toxicity in cats has been seen even with exposure to small amounts. Hypothermia may exacerbate the clinical effects of permethrin.

Clinical presentation

Almost all exposed cats will become symptomatic and the majority of these will display muscle tremors. Common clinical signs include muscle fasciculations, ear twitching, paw flicking, tremors, ataxia, seizures, hyperthermia and mydriasis. Effects on sensory nerves can result in hyperaesthesia and hypersalivation (which may also be seen after oral exposure). Clinical signs develop within 3 to 72 hours postexposure. Recovery takes from 2–3 days on average, but up to 5–7 days has been reported.

Diagnosis

Classic clinical signs are suggestive and owners should be questioned about exposure to flea treatments (either directly on the cat or on other animals in the household).

Management

For dermal exposures, the pet should be washed with warm water and washing-up liquid. Activated charcoal (to prevent absorption) is only indicated in confirmed oral exposures, as permethrin undergoes minimal enterohepatic recirculation (although other pyrethroids may be more extensively recirculated). Hypothermia, especially after bathing, must be prevented as it may exacerbate clinical signs by enhancing intracellular sodium movement.

The aim of drug therapy is to stop all seizure activity and decrease muscle tremors and fasciculations to a level unlikely to result in hyperthermia or muscle damage. Attempting to stop all muscle tremors with drug therapy may result in unnecessarily deep sedation/anaesthesia and respiratory depression. Methocarbamol (initial dose 44–220 mg/kg IV, given in small boluses of 30–40 mg/kg to a maximum of 330 mg/kg/day) should be used until tremors have improved or ceased. It is very efficacious for muscle fasciculations secondary to permethrin toxicity. If injectable methocarbamol is unavailable, it may be administered orally or the tablets may be ground up, dissolved in water and administered per rectum at the same doses used for intravenous administration.

Both benzodiazepines and phenobarbital may be used to attenuate clinical signs of tremors or seizures in combination with or instead of methocarbamol. Diazepam may be administered initially as IV bolus doses of 0.25–0.5 mg/kg and it may also be administered as a CRI of 0.2–0.5 mg/kg/hour. Phenobarbital should be administered in small doses of 2–4 mg/kg IV or IM as necessary, not to exceed 16 mg/kg/day. If necessary, propofol or alfaxalone CRI or gaseous anaesthesia may be used to anaesthetize the patient. NM blocking agents are not indicated.

Intravenous fluid therapy should be given to maintain hydration if the animal is unable to drink. More aggressive fluid rates may be indicated in the presence of myoglobinuria to minimize the possibility of myoglobinuria-induced nephropathy. Measurement of blood electrolytes will help to guide additional fluid therapy and choices (see Chapter 31).

The highly lipophilic nature of pyrethroids suggests that intravenous lipid administration may be an effective therapy to decrease the severity and duration of clinical signs.

Prognosis

The prognosis is good unless clinical signs have been present for a prolonged period prior to the institution of appropriate treatment; intensive supportive care may be necessary. Treatment delays or the presence of generalized seizures is associated with a worse prognosis and increases the likelihood of death. Death has been reported to occur in 5–37% of cases.

Salt toxicity (paintballs, play dough)

Overview

Sources of excess sodium include table salt (especially when used as an emetic), home-made play dough, paintballs, seawater and iatrogenic sources such as hypertonic saline solutions and sodium phosphate enemas.

Mechanism of action

An increase in serum sodium creates an increase in plasma osmolality. Water shifts from the interstitium to the vasculature, as well as from the intracellular fluid (ICF) to the ECF to maintain equilibrium. The ECF expands to a state of hypervolaemia, and dehydration of the cells results.

The lethal dose of sodium chloride is reported to be 4 g/kg PO, with clinical signs noted at dosages of approximately 1.9 g/kg PO. The level of resulting hypernatraemia seems to be a more accurate way of predicting clinical signs than the amount of sodium chloride ingested, with one study reporting seizures in all animals with serum sodium levels greater than 180 mmol/l (180 mEq/l).

Clinical presentation

Sodium chloride is a gastric irritant and ingestion of large amounts can lead to acute gastroenteritis and dehydration. Immediate clinical signs may include vomiting, polydipsia and polyuria. Ataxia, tremors, hyperthermia, seizures and death may be seen as a result of ICF shifts.

Diagnosis

A history of ingestion of sodium chloride-containing products and acute increases in serum sodium are strongly supportive.

Management

For recent exposure, induction of emesis is recommended. Activated charcoal is likely to be of little benefit and is not recommended.

Decreases in serum sodium must be monitored frequently and should not exceed 0.5–1.0 mmol/l/hour (mEq/l/hour). Acute elevations in serum sodium (i.e. within 2–4 hours) may be reduced more quickly than in animals with chronically elevated sodium, as the neurons have not had time to adjust osmolality. In the absence of a known time of ingestion, all hypernatraemic animals should be assumed to have chronic hypernatraemia (see Chapters 2 and 27). Rapid reduction in serum sodium levels can result in cerebral oedema and exacerbation of neurological signs if toxicity is chronic. The deficit of free water is calculated as:

$$\text{Free water deficit (l)} = 0.6 \times \text{body weight (kg)} \times (\text{patient's Na/normal Na} - 1).$$

The deficit should be replaced over the number of hours calculated to maintain a safe and slow decrease in sodium plasma levels, not to exceed 8–12 mmol/l (mEq/l) in a 24-hour period. 5% Dextrose in water is the fluid of choice for replacement of free water. Intravenous administration of 5% dextrose at up to 3.7 ml/kg/hour, in addition to regular isotonic maintenance fluids, should decrease serum sodium by approximately 1 mmol/l/hour (mEq/l/hour). Serum sodium and other electrolytes should be monitored at least every 4 hours and adjustments to fluid therapy made as needed. Combination with other isotonic fluids (lactated Ringer's solution, Normosol-R) is usually needed to prevent the sodium from dropping too quickly. If the neurological signs worsen, or sodium levels drop too quickly, free water supplementation should be temporarily discontinued and mannitol administered (0.5–1 g/kg IV) to treat cerebral oedema.

Increasing serum sodium concentrations can indicate inadequate decontamination. Repeat gastric lavage, or even surgical removal in extreme cases, has been recommended to remove ongoing sources of sodium. A loop diuretic (furosemide, 1–2 mg/kg IV) can be used to promote sodium excretion; however, it is important not to decrease sodium levels too quickly if this therapy is instituted.

Frequent access to small amounts of water may be sufficient to lower serum sodium levels in patients showing no clinical signs and only mild elevations in serum sodium concentration. Animals should not be allowed unlimited access to water at the risk of decreasing sodium too quickly.

Symptomatic and supportive care should be given as indicated.

Prognosis

The prognosis depends on the underlying cause, as well as the degree of hypernatraemia and associated clinical signs. Most animals treated appropriately with slow decreases in serum sodium will fully recover.

Sodium monofluoroacetate (1080)

Overview

Sodium monofluroacetate is also known as fluoroacetate, sodium fluoroacetate and SMFA. It is used for rodent, rabbit and carnivore pest control. Its use is restricted to authorized users in many countries; however, accidental poisonings do occur in baiting areas. Secondary poisoning occasionally occurs from ingestion of regurgitated baits or carcasses of baited animals.

Mechanism of action

Fluoroacetate is converted to fluorocitrate and blocks the tricarboxylic acid or Kreb's cycle. This impairs cellular respiration and energy metabolism, resulting in a lactic acidosis. The accumulation of citrate can bind serum calcium, resulting in low ionized calcium levels. The main organ systems affected are the GI, neurological and cardiovascular systems. The toxin is rapidly absorbed from the GI and respiratory tracts and may also be absorbed from mucous membranes and skin abrasions. Heat stroke could result in multiorgan failure and DIC in patients that survive the initial toxicity. The reported LD_{50} is 0.05–0.1 mg/kg in dogs and 0.2 mg/kg in cats.

Clinical presentation

Clinical signs generally occur 30 minutes to 2 hours post ingestion, although longer periods have been reported. Early signs include GI hypermotility (manifested by vomiting and diarrhoea), tenesmus, salivation, urination, anxiety and hyperaesthesia. Subsequent signs include muscle tremors, barking, howling or screaming, running fits and then generalized seizures (which can be interspersed with running fits) and eventually coma and death. Cardiac arrhythmias can occur due to cellular anoxia and hypocalcaemia. Hyperthermia may occur secondary to exertion, although hypothermia may occur in cats. Hypoxia and aspiration pneumonia may also be seen in exposed animals. In untreated cases death generally occurs within 2–12 hours from the onset of clinical signs.

Diagnosis

Diagnosis is based on the history of ingestion or exposure to an area that was recently (within 6 weeks) baited with 1080. Although 1080 is water soluble and broken down by many soil bacteria, dry, arid conditions may delay this breakdown and redistribution. Ionized hypocalcaemia combined with appropriate clinical signs is suggestive of exposure. Analysis of gastric contents can confirm exposure. Contents should be kept frozen until analysed to prevent bacterial breakdown of the toxin.

Management

Emesis should be induced and activated charcoal given if clinical signs have not yet developed. Patients who are already showing clinical signs should be anaesthetized and gastric and colonic lavage performed. Activated charcoal may be subsequently administered per os or via an orogastric tube and is an effective adsorbent for 1080.

To control seizures, patients should be kept anaesthetized; pentobarbital or propofol CRI is often recommended for the prolonged anaesthesia required. Ten to 48 hours of anaesthesia may be required until the patient is no longer showing clinical signs. Recovery from intravenous anaesthesia with pentobarbital may be confused with seizure activity, and it may be prudent to first wean the patient onto a shorter-acting anaesthetic, such as propofol, prior to attempting anaesthetic recovery.

One antidote treatment method, with a reported 83% success rate (5 of 6 dogs), is to administer 300 mg/kg of sodium bicarbonate IV (3.6 mmol/kg or 3.6 ml/kg of the 8.4% solution). Half is given as an intravenous bolus and the remainder over 20 minutes with intravenous fluids. This may result in the development of hypernatraemia. It is important, during this treatment, to monitor ventilation to avoid elevations in dissolved CO_2 levels.

Another antidote is acetamide; 15 g acetamide granules are dissolved in 1 litre of warmed 5% dextrose (consider the need for sterilization and infusion through a filter if made up from a chemical grade). The initial dosage is 10 ml/kg IV over 15 minutes, followed by an IV infusion at 8 ml/kg/hour until resolution of clinical signs. Hyponatraemia may develop during this therapy secondary to the large volumes of free water administered, and electrolytes should be closely monitored.

Calcium gluconate (5–15 mg/kg slow IV) should be administered as necessary if ionized hypocalcaemia develops. It is prudent to monitor for bradycardia (by ECG) during administration.

In addition, supportive care should be instituted.

Prognosis

The prognosis is guarded once seizures have developed. The mortality rate in dogs has been estimated to be close to 75%, but early aggressive therapy may improve this.

Strychnine

Overview

Strychnine is used as a pesticide for small mammals. Restricted access in many countries has decreased the incidence of unintended toxicity in companion animals.

Mechanism of action

Strychnine blocks the effects of the inhibitory neurotransmitter glycine in the spinal cord and prevents the release of glycine from Renshaw cells. This loss of inhibition leads to exaggerated neurological stimulation of muscle and severe muscular spasms. Reported LD_{50} doses are 0.5–1.2 mg/kg in dogs and 2 mg/kg in cats.

Clinical presentation

There is a rapid onset of clinical signs within 10–120 minutes after ingestion. Anxiety, tremors, muscular rigidity, muscular spasms, 'saw horse stance' of extensor rigidity and opisthotonus, and contracture of facial muscles may result in a 'sardonic grin' similar to that of patients with tetanus. Muscle spasms affect the respiratory muscles and diaphragm and death can occur from secondary hypoventilation, hypoxia or heat stroke.

Diagnosis

Baits may be specifically coloured in some countries and recognizable during gastric decontamination, or the history may be strongly suggestive. A definitive diagnosis generally requires analysis of gastric contents or tissue samples for the presence of strychnine or its metabolites.

Management

Emesis can be instituted if the animal has not yet developed any clinical signs of toxicity. It is contraindicated once clinical signs are present, due to the risk of inducing a generalized muscle spasm during the act of vomition, which could result in aspiration of stomach contents. Patients showing clinical signs are best anaesthetized for gastric lavage and administration of activated charcoal, which is an effective adsorbent for strychnine.

To control seizures and muscle activity, patients should be kept under sedation or anaesthesia for 24–72 hours until clinical signs resolve. For patients showing only mild clinical signs, benzodiazepines or phenobarbital may be control muscle spasms. For patients with moderate signs, methocarbamol may be used alone or as well as benzodiazepines and phenobarbital. Patients with severe clinical signs may require anaesthesia with CRI of propofol or pentobarbital.

Mechanical ventilation and associated supportive care may be required during treatment if deep anaesthesia or use of multiple muscle relaxants and sedatives is required for patients with severe clinical signs.

Prognosis

The prognosis is fair to guarded. If muscle spasms and tetany can be controlled with drug therapy, and supportive care and mechanical ventilation can be provided, the prognosis may be improved.

Neuroinhibitory toxins

Latrodectism (spider envenomation)

Overview

The *Latrodectus* genus of spiders is found throughout the world. The American black widow spider (*L. mactans*) (**399**) and the Australian red-back spider (*L. hasselti*) are the most notorious species. Females are significantly larger than males and responsible for envenomation. Female black widow spiders are easily recognized by the red or orange 'hourglass' present on the ventral or dorsal aspect of a shiny, dark abdomen and they can grow up to 2.5 cm long. Males are 20 times smaller than females and are unable to bite due to their small jaws. The red-back spider grows up to 1 cm in length and is black in colour with a red or orange stripe running from the dorsum to the ventral abdomen.

The venom and clinical signs of envenomation are very similar for all *Latrodectus* species.

Mechanism of action

The portion of the venom responsible for neurotoxic effects in dogs and cats is alpha-latrotoxin, which induces neurotransmitter release from nerve terminals. The net effect is a massive release of ACh, norepinephrine, dopamine, glutamate and enkephalins. At the pre-synaptic membrane, the toxin also irreversibly binds with the lipid bilayer of the cell membrane. This results in a cation selective channel and interferes with endocytosis of vesicle membranes. The LD_{50} of the black widow venom is 1.39 mg/kg, and a single bite can produce a fatal dose in companion animals. Studies show that the venom is capable of destroying local motor nerve terminals within 24 hours, with re-innervation and complete recovery occurring over the following 2–8 days.



▲ 399 A female black widow spider (*Latrodectus mactans*) showing the classic hourglass marking. (© Steve Ryan, used with permission.)

Clinical presentation

Clinical signs are generally seen within 8 hours of envenomation. In humans pain is the most significant clinical sign and without antivenom has been reported to last from days to months.

In dogs regional numbness, progressive muscle pain and fasciculations or cramping may be seen. Abdominal rigidity is also common. Restlessness is common due to the painful nature of the signs. Systemic signs can progress to hypertension, tachycardia, seizures and paralysis. Vomiting and diarrhoea may also occur.

Cats are more sensitive to spider venom and paralytic signs are often noted early after the bite. Hyperexcitability, pain, vocalization, excessive salivation, and restlessness are common. Vomiting and diarrhoea, muscle tremors, muscle fasciculations, cramping, ataxia and eventual flaccid muscle paralysis occur. Death is common in cats, with one study citing a 91% mortality rate.

Approximately 15% of bites are 'dry bites', in which no venom is injected.

Diagnosis

There are no confirmatory diagnostic tests for black widow or red-back spider envenomation. Historical information regarding noting the presence of these spiders in the environment can be supportive. Puncture wounds are often difficult to find due to the hair coat, small size and lack of a local tissue reaction. Diagnosis is usually dependent on onset of systemic clinical signs.

Management

Antivenom for black widow spider bites is available and provides the quickest relief of clinical signs (usually within 30 minutes of infusion). Severe pain is appropriate justification for the use of antivenom. Black widow antivenom should be diluted (in up to 100 ml of saline depending on patient size) and given IV over 30 minutes to 1 hour. Close monitoring for anaphylactoid reactions is imperative during infusion. Patients who develop a fever, tachycardia, hyperaemia or other signs of a reaction should have the antivenom temporarily stopped. Treatment with diphenhydramine (2–4 mg/kg SC) and resuming the infusion at a slower rate will usually allow for complete infusion of the antivenom.

Red-back spider antivenom is recommended for intramuscular administration, though intravenous administration is used in severe cases in humans. The rate of adverse reactions is rare in humans, with an incidence of 0.5–0.8%.

One vial is the recommended dose to treat intoxication by either spider, however, a second vial can be given if clinical signs recur. Black widow antivenom is supplied as a 2.5 ml vial (Merck) and red-back antivenom is supplied as a 500 U vial (1.0–1.5 ml) (CSL Ltd).

Red-back spider antivenom is effective even with delayed treatment and it is recommended for use up to 2 weeks postbite if clinical signs are still severe. Alternatively, supportive and symptomatic care to relieve clinical signs should be performed.

Administration of 10% calcium gluconate (1–3 ml/kg slowly IV at 4–6 hour intervals) may help control muscle cramping and fasciculations. If calcium infusion fails to maintain the patient for more than 1.5 hours, additional infusions are likely to be ineffective. Careful monitoring of heart rate and rhythm should be performed while administering calcium.

Pain medication (often opioids) is recommended to control the pain associated with envenomation and muscle cramping. Benzodiazepines are recommended and are often more successful at relieving muscle cramps and discomfort than are muscle relaxants (such as methocarbamol). BP should be monitored frequently, as patients are at risk of developing severe hypertension. There is a risk of respiratory depression from the venom and ventilatory support should be instituted in patients who are unable to ventilate adequately. Hospitalization and monitoring are recommended for a minimum of 48 hours.

Red-back spider antivenom has been shown to be effective for bites of the black widow spider and case studies and in-vitro studies show *Latrodectus* antivenoms have the ability to neutralize venoms of different *Latrodectus* species.

Prognosis

The prognosis for black widow envenomation is guarded. Clinical signs may persist for 3–7 days and complete recovery in severe cases may take weeks. The prognosis for red-back spider envenomation is fair to good if antivenom is administered.

Macadamia nuts

Overview

Macadamia nuts are cultivated in the USA (especially Hawaii) and Australia. They may be found in cookies (biscuits), candies (sweets) or nut mixes.

Mechanism of action

The toxic mechanism is unknown and has been limited to reports only in dogs.

Clinical presentation

Clinical signs usually develop within 12–24 hours of ingestion and most commonly involve hindlimb weakness, stiffness or paresis and muscle tremors. Vomiting, hyperthermia and depression may also be seen. Clinical signs have been seen in dogs ingesting as little as 0.7 g/kg of raw or roasted nuts and as much as 62.4 g/kg.

Diagnosis

There are no confirmatory tests available. Classic clinical signs are suggestive and questioning owners on potential exposure will generally elucidate the cause.

Management

Decontamination via emesis may be indicated in known, recent ingestion (within 2–4 hours). In general this is not indicated in patients who have already developed clinical signs. Supportive and symptomatic care should be instituted. Intravenous fluid therapy and anti-emetics may be considered in vomiting dogs. Intravenous fluid therapy and cooling measures should also be instituted in patients whose temperature is >40°C (>104°F).

Methocarbamol may be used to control muscle tremors and prevent further hyperthermia.

Prognosis

The prognosis is generally excellent, with most dogs making a full recovery within 48 hours.

Metronidazole

Overview

Metronidazole is commonly used to treat bacterial and protozoal infections in small animals.

Mechanism of action

The exact mechanism for metronidazole's neurotoxic effects is unknown; proposed mechanisms include inhibition of neuronal protein synthesis by binding to RNA and thiamine antagonism. Studies in dogs with metronidazole toxicity revealed axonal swelling and degeneration in vestibular nuclei, as well as leucomalacia of the brainstem. The toxic dose is generally stated as >60 mg/kg/day; however, lower dosages have been reported to cause neurotoxicity even after just a few days of administration.

Clinical presentation

Ataxia and vestibular signs (mostly bilateral), tremors, peripheral neuropathies and seizures are common manifestations of metronidazole toxicity. Vomiting, anorexia, stomatitis and glossitis may also be noted.

Diagnosis

A history of administration of metronidazole with consistent clinical signs provides supportive evidence of toxicosis. Discontinuation of therapy followed by resolution of clinical signs is also supportive.

Management

Discontinuation of metronidazole and supportive care are generally all that is necessary for treatment. Diazepam has been reported in dogs to hasten the recovery response times. Treatment with an initial dose of 0.2–0.5 mg/kg IV followed by 0.3–0.5 mg/kg PO q8h for 3 days can be considered in severely affected animals in an effort to promote resolution of clinical signs. Treatment with diazepam is not recommended in cats.

Prognosis

Metronidazole intoxication generally has an excellent prognosis, with most animals recovering completely within 14 days. Animals with severe CNS signs may take months to recover; however, this is very rare.

Snake bite envenomation

Overview

This section concentrates on Australian elapid envenomations; however, North American coral snake envenomation is also discussed.

In Australia, identification of specific snake species by members of the public is frequently inaccurate. Accurate choice of antivenom is determined by knowledge of local snakes, snake identification using a scale key or the most appropriate choice of antivenom determined by use of the Australian CSL Snake Venom Detection Kit. There are at least 25 terrestrial species of snake within Australia whose bite may require treatment with antivenom. The most significant genera responsible for envenomation include tiger snakes (*Notechis*) (**400b**), brown snakes (*Pseudonaja*), black snakes (*Pseudechis*) (**400c**), copperheads (*Austrelaps*), death adders (*Acanthophis*) (**400d**) and taipans (*Oxyuranus*).

Clinically significant North American coral snakes include subspecies of the *Micrurus* genus, including the Eastern coral snake (*M. fulvius fulvius*) (**400a**), the South Florida coral snake (*M. fulvius barbouri*) and the Texas coral snake (*M. fulvius tenere*). These snakes have red, yellow and black bands and the red bands contact the yellow bands.



▲ 400 **Venomous snakes. (a) An American coral snake (*M. fulvius fulvius*). (© Justin Oguni, with permission.) (b) A mainland tiger snake (*Notechis scutatus*). (c) A mulga snake (*Pseudechis australis*), also known as the 'king brown' snake, though actually a member of the black snake family. (d) A common death adder (*Acanthophis antarcticus*). (b, c and d © Brian Bush, with permission.)**

The basic principles of treatment of elapid envenomation are the same regardless of the snake species involved. Antivenom, if available, should be administered if the patient develops clinical signs of envenomation.

The venom of elapid snakes is composed of multiple different toxins; however, all elapids have neurotoxicity (paralysis) as a common clinical sign. In general, it is rare to find the bite site in animals because of the snake's small fangs and minimal local tissue damage associated with bites by these species in comparison with pit vipers (rattlesnakes). In Australia, snake bites occur during the warmer months of the year and are rare in winter. Specific antivenom is required for envenomation by individual snake species and an incorrect choice of antivenom will not be efficacious.

Mechanism of action

Toxins from Australian venomous snakes have the following effects:

- **Neurotoxins.** These cause neuromuscular paralysis either presynaptically by preventing ACh release or postsynaptically by binding to AchRs. Eventually, death occurs due to respiratory paralysis.
  Presynaptic neurotoxins cause structural changes to the nerve terminal, which with time becomes unresponsive to antivenom.
- **Procoagulants.** These cause diffuse activation of coagulation, resulting in widespread thrombus formation, which generally resolves by fibrinolysis. Clinically, a severe coagulopathy secondary to consumption of clotting factors is seen; this affects both intrinsic and extrinsic coagulation pathways. Coagulopathy is unresponsive to fresh frozen plasma until procoagulants have been effectively neutralized with antivenom.
- **Anticoagulants.** Have a heparin-like effect and cause mild prolongations in aPTT without development of clinical bleeding.
- **Haemolysins.** Damage red cell membranes, causing intravascular haemolysis.
- **Myotoxins.** Damage striated skeletal muscle, resulting in diffuse rhabdomyolysis.

North American coral snake venom contains several neurotoxins that cause postsynaptic blockade at the NM junction.

Venom absorption occurs via the lymphatics and muscular activity can hasten the clinical signs of envenomation.

Clinical presentation

Australia

Clinical signs vary according to the snake species:

- Tiger snakes: paralysis, coagulopathy, rhabdomyolysis, mild haemolysis.
- Brown snakes: paralysis and coagulopathy.
- Death adders: paralysis.
- Black snakes and copperheads: haemolysis, rhabdomyolysis, paralysis (occasionally mild weakness only), bite site swelling +/- coagulopathy.
- Taipans: paralysis, rhabdomyolysis, coagulopathy.

Lack of coagulopathy does not rule out envenomation by any of these species.

Preparalytic signs

Salivation, vomiting, dyspnoea, acute collapse, inappropriate urination or defecation may occur first. These temporary signs generally occur within 15 minutes of the snake bite, before being followed by a period of recovery. Dogs that develop preparalytic signs after a bite by a highly venomous Australian snake generally go on to develop life-threatening signs of envenomation. Antivenom should be administered to animals that have a history of preparalytic signs post snake bite.

Lower motor neuron paralysis

LMN signs commonly start with weakness of the palpebral and gag reflexes and progress to weakness and ataxia in the hindlimbs, then the forelimbs and finally the respiratory muscles. Dyspnoea secondary to saliva pooling in the paralysed pharynx is common, as is laryngeal paralysis, and can occur before generalized paralysis develops. Onset can be rapid, with some animals requiring intubation and ventilation within 30 minutes of being bitten; however, in some animal reports, the development of NM paralysis may be delayed by up to 24 hours. Aspiration pneumonia may occur as a sequela of pharyngeal and laryngeal paralysis. Pupillary dilation and loss of PLR occur as later signs.

Coagulopathy
Prolongations in PT, aPTT and ACT can occur. In humans, thrombocytopenia is also reported. Clinical coagulopathies with overt bleeding are uncommon except in brown snake bites. However, patients may develop severe bleeding in any area of the body associated with venipuncture (avoid jugular venipuncture and use peripheral veins when possible). Haematemesis and haemorrhagic diarrhoea occasionally occur, as well as haematuria, epistaxis and hyphaema. Spinal cord compression secondary to epidural haematoma has also been reported.

Rhabdomyolysis
Myoglobinuria may be severe and can result in acute renal failure. Additionally, if insufficient antivenom is administered, there can be significant damage to skeletal muscle. Megaoesophagus may occur in dogs, with recovery times of up to 5 weeks reported. CK levels may increase to 10,000–1,000,000 U/l.

Haemolysis
Red cell lysis results in haemoglobinuria. Clinically significant anaemia generally only occurs with black snake bites; however, the presence of haemolysis can be used as an indication of envenomation.

Acute renal failure
Acute renal failure may occur secondary to myoglobinuria, haemoglobinuria or ischaemia.

North America
Coral snake envenomation results in generalized LMN paralysis. The onset may be rapid or delayed up to 18 hours. The neurological signs are the same as for Australian snakes (see above). In dogs, haemolytic anaemia, haemoglobinuria and elevations in CK also occur.

Diagnosis
Bite sites are infrequently found due to the snake's small fangs, the lack of swelling and the animal's hair coat. Appropriate clinical signs of envenomation and recent known contact with a snake, or a history of snakes in the animal's environment, are highly suggestive of envenomation.

Management
First-aid advice to owners is to keep animals quiet and rested to slow the onset of clinical signs. Immediate transport to a veterinary hospital is indicated even if the animal appears asymptomatic. Onset of respiratory paralysis can be extremely rapid in severe envenomations. Owners should be advised to position paralysed animals so as to maintain an open airway and with the head lowered to enable drainage of saliva. If cyanosis and respiratory arrest develop, owner-administered mouth-to-nose breathing may maintain life during transport.

If bites occur on a distal limb, a crepe pressure bandage applied to the whole limb can significantly slow the onset of clinical signs. Most animals are bitten on the head, neck or thorax, and these sites are not suitable for pressure bandage application.

On arrival at the veterinary hospital, animals must never be left unattended due to the occasional rapid onset of paralysis and respiratory arrest. The bite site should not be washed, as it may help in identification of the appropriate antivenom to administer. Bite site infection is extremely uncommon. Intravenous catheterization should be performed immediately. Blood is collected for coagulation testing from the catheter where possible. Alternatively, a compression bandage should be applied at sites of blood collection. Animals should be strictly confined and rested until recovered. Two weeks' rest is recommended after discharge.

In Australia, a history of preparalytic signs provides an indication for antivenom administration even if there is no other clinical evidence of envenomation. The appropriate antivenom in Australia can be determined by visual identification of the snake using scale keys or by an experienced herpetologist. The Australian CSL Snake Venom Detection Kit can be used on the bite site, urine or blood. (*Note:* A positive response to this kit alone does not indicate antivenom is required. The animal must also have clinical signs of envenomation.) Knowledge of local snake species can also help guide antivenom choices.

A neurological examination should be performed, recorded and repeated hourly in asymptomatic animals. The development of any signs of weakness or paralysis is an indication for antivenom. Coagulation testing (PT and aPTT or ACT) should be performed and repeated every 2–6 hours. The development of a coagulopathy is an indication for antivenom. Coagulopathies normally take at least 6 hours to start to improve after antivenom. CK should be measured and repeated every 6 hours. Significant elevations of >1,000 U/l are an indication for antivenom. Myoglobinuria should start to clear after sufficient antivenom has been administered.

Urine should be collected to check for casts, glucose, haemoglobin/myoglobin and red cells. The presence of casts or glucose (in a normoglycaemic patient) is an indication of renal damage and monitoring or treatment for acute renal failure may be required. The presence of myoglobinuria/haemoglobinuria may be an indication of envenomation. Patients with dark red or brown/black urine should be closely monitored for the development of acute renal failure and treated aggressively if oliguria or anuria develops.

Patients that develop clinical signs should be placed on intravenous fluids at 2–3× maintenance to minimize the development of acute renal failure secondary to myoglobinuria or haemoglobinuria. Fluid diuresis should be instituted as snake venom toxins are excreted in the urine. Mannitol should be administered if oliguria or anuria develops in well hydrated patients. Antivenom-induced anaphylaxis may also require aggressive fluid therapy.

Animals that present with or develop dyspnoea may require intubation, using anaesthesia as required. Mechanical ventilation should be used in patients with elevated $P'ETCO_2$ or minimal respiratory excursions. Other causes of dyspnoea, such as overhydration in the face of renal failure, should be ruled out. Shock may develop secondary to hypoxia.

Antivenom is dosed according to the amount of venom injected rather than the animal's body weight. Each vial of antivenom has sufficient antibodies for an average bite. Animals with preparalytic signs or mild signs generally only require 1 vial of antivenom. Animals with respiratory paralysis generally require at least 2–4 vials of antivenom, which should be given within the first 1–2 hours of treatment. If the animal continues to deteriorate, more antivenom should be administered and steps taken to confirm the envenomating snake species if this has not already occurred.

The correct antivenom is required for the specific snake species involved. The following is a list of snake species venom treated by specific antivenoms:

- Tiger snake antivenom is used for the common tiger snake (*Notechis scutatus*), black tiger snake (*Notechis ater*), common copperhead (*Austrelaps superbus*), highland copperhead (*A.ramsayi*), pygmy copperhead (*A.labialis*), rough-scaled snake (*Tropidechis carinatus*), broad-headed snake (*Hoplocephalus bungaroides*), Stephens' banded snake (*Hoplocephalus stephansii*), red-bellied black snake (*Pseudechis porphyriacus*) and the spotted black snake (*Pseudechis guttatus*). It may also be suitable for North American coral snake envenomation.
- Brown snake antivenom is used for all members of the brown snake family *(Pseudonaja)* including the eastern brown snake *(P. textilis)*, western brown snake *(P. nuchalis)*, dugite (*P. affinis*), peninsula brown snake (*P. inframacula*), spotted brown snake (*P. gutta*) and Ingram's brown snake (*P. ingrami*).
- Black snake antivenom is used for only a few members of the black snake family including the mulga, also known as the king brown snake (*Pseudechis australis*), Collett's snake (*P. colletii*), and Butler's mulga snake (*P. butleri)*. Some members of the black snake genus (e.g. the red-bellied black snake) can be treated adequately by tiger snake antivenom.
- Death adder antivenom is used to treat envenomations by the common death adder (*Acanthophis antarcticus*), northern death adder (*A. praelongus)*, desert death adder (*A. pyrrhus*), pilbara death adder (*A. wellsii*) and the bardick (*Echiopsis curta*).
- Taipan antivenom is used to treat the common taipan (*Oxyuranus scutellatus*) and the inland taipan (*O. microlepidotus*).
- Polyvalent antivenom treats all venomous Australian snakes.

Novel snake species causing clinically significant envenomation are ideally treated with antivenom according to the CSL Snake Venom Detection Kit results or, alternatively, with tiger snake antivenom or polyvalent antivenom if available.

Production of the coral snake antivenom (Antivenom [*Micrurus fulvius*] [Equine]) has been discontinued and there is currently no alternative product available in the USA. Alternatives that show cross-reactivity include Australian tiger snake antivenom and Mexican coral snake (*Micrurus*) antivenom. One to 4 vials of coral snake antivenom are recommended for treatment. The dose is determined by symptom severity and amount of venom injected. Very small animals or animals that deteriorate after initial treatment will require higher doses.

Supportive care should be instituted as described in the tick paralysis section below.

Prognosis

In Australia, following treatment with antivenom, 91% of cats and 75–92% of dogs have been reported to survive snake envenomation.

Tetrodotoxin

Overview

Tetrodotoxin is found in fish of the family Tetraondontidae (scaleless fish with four large teeth). These sea fish are found throughout the world. Various species of tetrodotoxic fish may also be known as puffer fish, blowfish, blowies, globefish, toadfish (**401**) and porcupine fish. Some species have spines and inflate their bodies when startled. Tetrodotoxin is also found in the bite of the blue-ringed octopus (*Hapolochlaena*) of Australia, central American frogs of the *Aetolopus* genus, Californian newts of the *Taricha* genus and the Pacific goby, as well as various other marine animals. Tetrodotoxin levels vary seasonally and between species.



▲ 401 Toadfish. (© Helena Lemin, used with permission.)

Dogs most commonly become intoxicated by eating fish discarded by fishermen on beaches and tidal river banks. Cats become intoxicated when mistakenly fed fish caught by their owners.

Mechanism of action

Tetrodotoxin blocks sodium channels thus preventing the generation of action potentials. Peripheral nerve fibres are mainly affected, but autonomic nerves, sensory nerves, skeletal muscles and, least commonly, cardiac muscle can also be affected. This results in generalized LMN paralysis, hypoventilation or respiratory arrest, vasodilation and hypotension. Stimulation of the chemoreceptor trigger zone causes vomiting.

The lethal oral dose in dogs is 70 µg/kg; when administered subcutaneously the lethal dose is 15 µg/kg; an intravenous dose of 0.3 µg/kg will result in emesis. In cats the lethal intravenous dose is 2 µg/kg.

Clinical presentation

Onset of clinical signs can be within 10 minutes to 1 hour of ingestion, but may be delayed for hours after ingestion; one report documented a delay of 24 hours before a dog exhibited paralysis.

In dogs, early signs include severe vomiting, which is often sufficient to cause adequate gastric decontamination, probably preventing absorption of lethal levels of the toxin. However, if vomiting is ineffective at decontamination or a high dose has been absorbed, dogs may go on to develop salivation, weakness, ataxia, facial paralysis and generalized muscle paralysis, which in the most severe cases can include respiratory paralysis. Skeletal muscle fasciculations have also been reported in a study of the effects of tetrodotoxin in dogs.

In cats, cases of ataxia without respiratory failure, as well as death, have been reported. Death is generally due to respiratory paralysis and can occur as rapidly as 17 minutes after ingestion. Hypotension is uncommon.

Diagnosis

Diagnosis is based on a history of known or suspected tetrodotoxic fish ingestion and a rapid onset of LMN paralysis. Liquid or gas chromatography of gastric contents, serum or urine will help confirm the diagnosis.

Management

Emesis or gastric lavage is indicated in animals that have not vomited. Activated charcoal should be administered. Supportive care is indicated if there is respiratory paralysis – oxygen if hypoxaemic, mechanical ventilation if hypoventilating. Generally, patients who require supplemental oxygen will also require ventilation. Hydration should be maintained with intravenous fluids if affected animals have evidence of pharyngeal or oesophageal paralysis. Hypotension is initially treated with intravenous fluids and then inotropes or vasopressors if required. Ventilation may be required for up to 3 days, although most animals require ventilation for less than 12 hours.

Humans frequently remain mentally aware during severe paralysis, and sedation to minimize anxiety should be used in paralysed animals during ventilation. Drugs that could predispose to hypotension should not be used.

Prognosis

The majority of animal cases recover within 2–3 days. The prognosis is grave if respiratory paralysis develops and mechanical or manual ventilation is not rapidly provided. The prognosis is fair if animals develop paralysis without respiratory failure. The prognosis for survival can be good if the animal is still breathing when it reaches veterinary care and appropriate intensive care is provided.

Tick paralysis (Australia)

Overview

Tick paralysis is a common problem affecting domestic animals living along the east coast of Australia. Cases of tick paralysis most commonly occur from spring to midsummer, although they can occur at any time of year.

Mechanism of action

Neurotoxins (holocyclotoxins) are produced in the salivary glands of female *Ixodes holocyclus* ticks (**402**) and injected during feeding (**403**). The toxin prevents release of ACh at the NM junction. Cardiotoxicity occasionally occurs and is clinically associated with diastolic dysfunction due to impaired myocardial relaxation. The presence of additional ticks prevents recovery despite administration of tick antitoxin serum. Clinical signs can continue to progress for up to 48 hours after tick removal if tick antitoxin serum is not administered. Immunity develops in some dogs and tick antitoxin serum is produced from serum collected from hyperimmune dogs.

Clinical presentation

The onset of clinical signs generally occurs within 5–7 days (and rarely up to 2 weeks) of tick attachment; if the ticks remain attached and no treatment is provided, death occurs 18–32 hours later.

Animals with tick paralysis present with a combination of LMN paralysis and respiratory depression. Occasionally, animals will present with vomiting or regurgitation as the only clinical sign. Several slightly different scoring systems have been used to stage the progressive deterioration of clinical signs:

- Gait score:
  - No gait abnormalities or mild ataxia when walked.
  - Significant ataxia present, but ambulatory.
  - Non-ambulatory, but can maintain sternal position and manoeuvre into sternal position from lateral recumbency.
  - Laterally recumbent and unable to manoeuvre into sternal recumbency; can weakly move all limbs.
  - Moribund.



▲ 402 Tick (*Ixodes holocyclus*): ventral aspect on left and dorsal on the right. (© Simon Lemin, used with permission.)



▲ 403 (a) Paralysis tick (*Ixodes holocyclus*) attached to skin. (© Simon Lemin, used with permission.) (b) The appearance of a tick bite on a dog after removal of the tick (the 'tick crater').

- Respiratory score:
  - Normal. Normal character and rate (<30/minute).
  - Mild compromise. Increased rate (≥30/minute), normal respiratory pattern or mild expiratory effort.
  - Moderate compromise with abnormal respiratory expiratory grunt. Gasping and cyanosis may be present. Respiratory rate may be decreased (i.e. ≤12/minute).
  - Severe compromise with dyspnoea and 'grunting' respiration due to vocal cord closure during expiration.

Focal neurological deficits, such as localized facial paralysis, can occur with ticks found ipsilaterally on the head or neck. Other neurological signs include changes in the sound of vocalization (bark or meow), pupillary dilation and loss of PLR, palpebral paralysis, decreased gag reflex, facial paralysis, bladder paralysis, gagging and retching. Salivation and retching are common due to pharyngeal and oesophageal dysfunction. Megaoesophagus is a common finding on thoracic radiographs (70% of cases). Vomiting also occurs. Hypoventilation secondary to respiratory paralysis occurs late in the disease. During the final stages, hypoxaemia and hypercapnoea develop. Hypoxaemia is not solely due to hypoventilation and can be contributed to by either aspiration pneumonia or pulmonary oedema. Respiratory compromise is significantly associated with mortality. Laryngeal paralysis may cause clinically significant upper airway obstruction.

Reported cardiovascular abnormalities include prolonged QT intervals and altered T wave morphology on ECG analysis. These changes temporarily persist after apparent recovery. Rarely, increased systemic mean and systolic arterial pressure is observed and in-vivo studies have shown increases in pulmonary artery pressure.

Diagnosis

The presence of an *Ixodes holocyclus* tick and appropriate clinical signs confirm the diagnosis. Even if no evidence of a tick or tick crater (attachment site) is found, the presence of appropriate clinical signs in an animal that has been in an endemic area within the previous 2 weeks is regarded as strongly suggestive of tick paralysis and an indication for treatment if no other cause is diagnosed.

Management

All ticks should be removed. The whole animal's coat should be repeatedly searched for the presence of additional ticks and insecticides effective against ticks should be applied. In long-haired animals, close clipping of the coat may be required (after treatment with antiserum and stabilization). Ticks are most commonly found around the head, neck and shoulders, but they can be found anywhere on the body or external orifices.

Animals that have no clinical signs should be monitored closely and tick antitoxin serum administered if required. Tick antitoxin serum should definitely be administered to animals that have significant ataxia, paralysis or any respiratory compromise.

Clinical improvement generally lags at least 12 hours behind hyperimmune serum administration. In some patients there is a mild deterioration in this period before improvement is seen. Tick antitoxin serum should be warmed, diluted in saline and administered slowly IV (over 1 hour) while the animal is monitored closely for anaphylaxis. Antihistamines, corticosteroids or adrenaline (epinephrine) are administered as premedication at the veterinarian's discretion. Because the antitoxin serum is produced from the serum of hyperimmune dogs, there is a potential risk of anaphylaxis or anaphylactoid reactions. The recommended dose of tick antiserum is generally 1 ml/kg, with a minimum of 5–8 ml and a maximum dose of 25 ml. The higher end of the dosage rate is recommended for cases with severe clinical signs or multiple ticks present.

Three percent of dogs and 6% of cats treated by general practitioners have been reported to develop adverse reactions to the administration of tick antitoxin serum, with one study attributing the majority of reactions to the Bezold–Jarisch reflex (bradycardia and hypotension) rather than anaphylaxis. Slow administration of antiserum minimizes the risk of non-anaphylactic reactions developing.

Adrenaline and possibly antihistamines or corticosteroids should be available for administration if anaphylaxis develops.

After recovery, a 2-week convalescence period with minimal exercise is recommended, as exercise-induced sudden death occasionally occurs. At discharge, owners should be counselled on tick preventive measures and the importance of daily manual searching of the animal's coat for ticks in endemic areas.

Supportive care for paralysis should include:

- Strict confined rest.
- Recumbent animals should be kept on padded bedding and turned every 4 hours to prevent pressure sores.
- Food and water should be withheld until animals are fully recovered and have had no episodes of vomiting or regurgitation for 24 hours.
- Hydration should be maintained with intravenous fluids, but fluid overload must be avoided as there may be an increased risk of development of pulmonary oedema. Mild cases in healthy young animals who recover within 24 hours may not require intravenous fluids, provided no signs of dehydration develop.
- Normothermia must be maintained.
- Bladder size should be monitored and the bladder should be expressed manually or catheterized to prevent overdistension and subsequent bladder atony.
- Corneal hydration should be maintained with the use of ocular lubricants if the blink reflex is compromised.
- Animals should be sedated if distressed: opioids, benzodiazepines or acepromazine can be used.
- Animals should be positioned in sternal recumbency wherever possible. In animals unable to maintain sternal recumbency the shoulders should be elevated above the stomach and the head positioned to optimize drainage of saliva and thus minimize the risk of aspiration. Pharyngeal and oesophageal suctioning is frequently required in recumbent animals. Intubation with a cuffed endotracheal tube should be considered in severely paralysed patients at significant risk of aspiration.
- Metoclopramide CRI (1–2 mg/kg/day) can be administered as a prokinetic to try to minimize vomiting and aspiration.

Supportive care for respiratory signs should include:

- Oxygenation should be monitored and oxygen administered if hypoxia develops, commonly by the intranasal route or oxygen cage.
- Mechanical ventilation will be required if respiratory paralysis and hypoventilation occur.

- Aspiration pneumonia is a common complication and should be treated appropriately with parenteral antibiotics (ideally based on culture and sensitivity testing) and intravenous fluids.
- Pulmonary oedema may also occur secondary to congestive heart failure. Radiographs and echocardiography should be used to confirm congestive heart failure prior to treatment with diuretics.
- Patients with laryngeal paralysis may develop significant upper airway obstruction. Sedation may alleviate distress; however, intubation or tracheostomy and oxygen insufflation will be required in severe cases.

Prognosis

Mortality rates following treatment with tick antitoxin of 5% in dogs and 0.6% in cats have been reported.

Tick paralysis (North America)

Overview

The ticks most commonly associated with tick paralysis in North America are the Rocky Mountain wood tick (*Dermacentor andersoni*), the American dog tick (*Dermacentor variabilis*), the Lone star tick (*Amblyomma americanum*) and the Gulf coast tick (*Amblyomma maculatum*). Dogs are most frequently affected, whereas cats do not seem to develop signs of this disease in spite of tick attachment.

Mechanism of action

The toxin appears to inhibit ACh release at the NM junction of motor nerves. Sensory nerve conduction may also be affected.

Clinical presentation

Ascending LMN paralysis develops within 5–9 days of tick attachment. One tick is sufficient to cause paralysis; large numbers of ticks are associated with increased severity of clinical signs and rapidity of onset. Early signs are hindlimb weakness and ataxia, which progress to quadriplegia over 1–3 days. If ticks remain *in situ*, death from respiratory paralysis may occur in 1–5 days. A change in the bark suggestive of laryngeal paralysis may occur, but otherwise CN paralysis rarely occurs.

Diagnosis

Diagnosis is based on appropriate clinical signs and the presence of an engorged tick, together with rapid improvement after tick removal.

Management

The entire tick, including the mouth parts, must be removed. Repeated searching of the whole body for further ticks should be carried out. Long hair should be clipped to improve the efficacy of tick searches. Application of topical insecticidal solution effective against ticks is indicated. Noticeable improvement occurs within 24 hours of tick removal and the majority of cases are fully recovered within 1–3 days if all ticks are removed.

Supportive care for paralysis is described above in the section on tick paralysis in Australia.

Prognosis

The prognosis is good if all ticks are removed and animals do not require ventilatory support.

PART 4

SPECIFIC MANAGEMENT ISSUES

CHAPTER 29 Emergency neuroanaesthesia

CHAPTER 30 Analgesia for patients with neurological disease

CHAPTER 31 Fluid therapy

CHAPTER 32 Postoperative supportive care and physical rehabilitation

APPENDICES

EMERGENCY NEUROANAESTHESIA

Anthea Raisis & Gabrielle Musk

INTRODUCTION

This chapter discusses the considerations and techniques for anaesthetizing animals with neurological disease. The chapter will cover intracranial disease, spinal disease and NM disease. A thorough understanding of the pathophysiology of diseases affecting these regions of the nervous system is essential to select the most appropriate anaesthetic technique and drug combination.

INTRACRANIAL DISEASE

Considerations

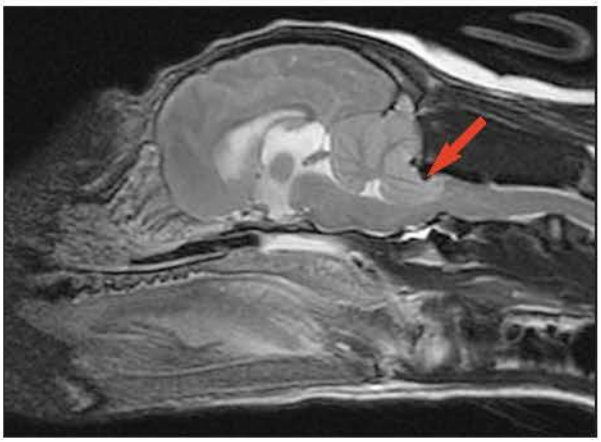
The main aim of anaesthesia in animals with intracranial disease is to preserve neuronal function. Normal neuronal function depends on maintaining adequate CBF.

CBF regulation is complex and will not be described in detail in this chapter (for more details see Further reading). Put simply, CBF is maintained if CPP is maintained. The CPP represents the difference between MAP and ICP. The considerations for maintaining CBF and minimizing neuronal injury during anaesthesia will be discussed with reference to the stages of the anaesthetic procedure (stabilization, induction, maintenance and recovery from anaesthesia). This is summarized in *Table 99* (p. 537).

Stabilization prior to anaesthesia

Any patient with increased ICP (**404**), regardless of the cause, requires stabilization before considering anaesthesia or sedation for further diagnostics.

Correction of hypoxaemia, hypercapnia and poor perfusion are the most important strategies for reducing ICP and stabilizing the patient prior to anaesthesia. (For specific details on supporting the respiratory and cardiovascular systems see Chapter 2.)



▲ 404 **Animals with intracranial disease are at risk of increased ICP and subsequent brain herniation (as shown on this sagittal T2-weighted MR image [arrow]) if appropriate stabilization is not performed prior to anaesthesia. (Photo courtesy Victoria Johnson)**

Specific management of increased ICP is indicated if deterioration of neurological status occurs rapidly or continues despite normal oxygenation, ventilation and perfusion. (For management of increased ICP see Chapter 20.)

Sedation

In animals with clinical signs of intracranial disease, the performance of procedures under heavy sedation is generally avoided. Heavy sedation may lead to excessive depression of cardiovascular and respiratory function,



▲ **405** **Heavy sedation, as seen in this Bull Terrier, is generally avoided in patients with intracranial disease, due to the risk of excessive cardiovascular and respiratory depression.**

which will exacerbate secondary neuronal injury (**405**). In addition, heavy sedation may interfere with accurate assessment of the neurological status of the animal and delay initiation of appropriate therapy.

In these cases, anaesthesia performed carefully with a good understanding of how to minimize detrimental effects is preferable, as this allows protection of the airway and control of ventilation. In addition, many anaesthetic agents, such as propofol and barbiturates, have the added benefit of reducing cerebral metabolic rate, which helps reduce neurological injury.

Premedication

The aims of premedication are to:

- Reduce stress and anxiety.
- Decrease the amount of anaesthetic induction and maintenance agents required.
- Provide analgesia.

Agents used for premedication should have minimal effects on cerebral perfusion and ICP. The advantages and disadvantages of different agents in animals with intracranial disease are detailed in *Table 100* (p. 539). Drugs such as acepromazine and medetomidine are best avoided in animals with intracranial disease.

Opioids provide analgesia and varying degrees of sedation without affecting cerebral perfusion or ICP. Adverse effects associated with a decrease in heart rate and respiratory depression can be avoided by using conservative doses. Morphine administration is best avoided in patients with high ICP given its significant potential for causing vomiting (and transient increases in ICP).

Benzodiazepines may be useful as anxiolytics in critically ill animals. These agents should be used cautiously in animals with mild disease/minimal decreases in mentation, as the effects can be unreliable and excitement, dysphoria and disinhibition can occur.

Phenobarbital is the drug most often used to control seizures. The authors have found that the administration of phenobarbital at 2–3 mg/kg intramuscularly can be a useful premedicant in anxious dogs when used in conjunction with an opioid 30 minutes prior to induction of anaesthesia.

Adjustment of dose rates of sedative and anaesthetic agents

In animals with intracranial disease, damage to the blood–brain barrier and concurrent CNS depression due to the neurological injury will serve to exacerbate the effects of a given dose of anaesthetic or analgesic agent. As a result, the doses used in these patients should be lower than those used in healthy patients. As the agents have a rapid onset and short duration of action, the dose rate can be adjusted incrementally (i.e. titrated to effect) until the desired analgesic effect is achieved, while minimizing side-effects.

Induction of anaesthesia

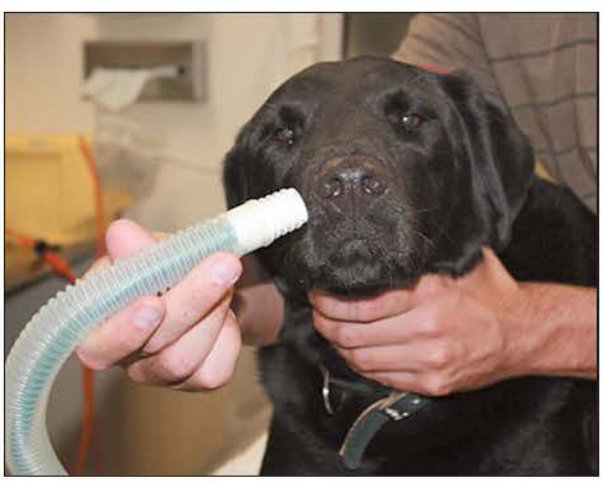
A smooth and high-quality induction of anaesthesia is essential. Minimizing stress and struggling and maintaining oxygenation and ventilation during induction of anaesthesia is necessary to prevent adverse effects on the CNS. The induction of anaesthesia using intravenous agents minimizes struggling and allows rapid control of the airway.

Pre-oxygenation is performed by mask, if tolerated, or by flow-by (**406**) for 5–10 minutes prior to induction to minimize hypoxaemia during and immediately following induction of anaesthesia.

Table 99 Considerations for anaesthetizing animals with intracranial disease

CONSIDERATION	MANAGEMENT
Maintain adequate CPP (CPP = MAP – ICP)	Maintain MAP between 80 mmHg and 100 mmHg. Maintain normal circulating blood volume. Minimize depressant effects of anaesthetic agents on cardiovascular function. Avoid/use carefully anaesthetic drugs that interfere with CBF autoregulation (e.g. volatile anaesthetics)
Maintain haemodynamic stability	Avoid sudden increases in MAP and associated increases in ICP caused by stress, pain, surgical stimulation and laryngeal stimulation. Provide adequate analgesia. Ensure adequate depth of anaesthesia before intubation
Ensure adequate ventilation and normocapnia ($\boldsymbol{P}aCO_2$ 35–40 mmHg)	Avoid hypercapnia ($\boldsymbol{P}aCO_2$ >40 mmHg) and associated increased ICP. Use positive pressure ventilation during anaesthesia. Avoid hyperventilation ($\boldsymbol{P}aCO_2$ <30 mmHg) except in an emergency to avoid brain herniation. Do not decrease $\boldsymbol{P}aCO_2$ below 30 mmHg
Maintain adequate oxygenation	Avoid hypoxaemia (PaO_2 <80 mmHg) by providing oxygen supplementation during induction, maintenance and recovery from anaesthesia
Decrease CMR	Select anaesthetic agents that decrease CMR (e.g. propofol). Avoid increase in CMR by preventing or controlling seizures, maintaining normothermia and avoiding anaesthetic agents that increase CMR (e.g. ketamine)
Ensure adequate venous drainage	Avoid interference with jugular venous blood flow and associated venous congestion and increased ICP. Avoid jugular obstruction, excessive airway pressure during ventilation and fluid overload. Mild head elevation (15–30 degrees) will encourage venous drainage

MAP = mean arterial blood pressure; ICP = intracranial pressure; CBF = cerebral blood flow; CMR = cerebral metabolic rate; $PaCO_2$ = arterial carbon dioxide partial pressure.



◀ 406 'Flow-by' oxygen therapy is useful for providing oxygen supplementation to animals that will not tolerate a mask over their face.

Manual ventilation with a close-fitting mask during induction of anaesthesia (**407**) may be necessary to ensure normocapnia until the anaesthetic depth is sufficient to minimize reflex responses (i.e. cough, increased heart rate and MAP) to endotracheal intubation. Once an oral ETT has been positioned and secured in place, ventilation via the tube is commenced. (*Note:* When ventilating via a mask, oxygen can be forced into the stomach, leading to gastric distension. Should this occur, a stomach tube can be passed once the animal is adequately anaesthetized and the stomach deflated.)

To maintain adequate cardiovascular and respiratory function during induction of anaesthesia, the use of short-acting agents that can be carefully titrated to effect without excitation is preferred. Drugs that minimally interfere with regulation of cerebral perfusion are also preferred. The advantages and disadvantages of different intravenous anaesthetic agents in the neurological patient are provided in *Table 100*. Propofol is the agent the authors most frequently use in animals with intracranial disease. The administration of 'co-induction' agents with fewer depressant effects on the cardiovascular and respiratory systems can be used to reduce the dose of the more depressant induction drugs. Co-induction agents (see *Table 101*, p. 540) are administered immediately prior to the induction agent and are usually given intravenously.

To minimize coughing in response to endotracheal intubation, it is important to ensure that the depth of anaesthesia is adequate. The depth of anaesthesia required to prevent a response to intubation is comparable to that required for major surgery. It is common practice in cats to apply topical local anaesthetic (lidocaine) to the larynx before intubation (**408**). This is particularly effective for preventing the autonomic response to intubation and it is useful for canine patients as well. In canine patients, use of co-induction agents such as lidocaine (1–2 mg/kg) and opioids (e.g. fentanyl, 1–5 μg/kg) intravenously can also help reduce stimulation of the larynx during intubation.



◀ **407** Ventilation via a tight-fitting mask may be necessary during induction to ensure adequate CO_2 removal and delivery of oxygen.

▼ **408** Application of topical lidocaine to the cat's larynx, after an adequate depth of anaesthesia has been achieved.



Table 100 **Intravenous sedatives and induction agents for use in animals with central nervous system disease**

AGENT	CBF REGULATION	DIRECT CARDIOVASCULAR EFFECTS	CMR	ICP	SEIZURE ACTIVITY	COMMENT	DOSE RATE*
Acepromazine	NR	↓↓ BP	NR	↑	↑	Avoid in intracranial disease. Useful anxiolytic in spinal disease. Contraindicated in hypovolaemic patients	0.01–0.05 mg/kg IM
Alpha-2 agonists	↓ Flow-metabolic coupling	↑ BP then ↓BP	↓	-	↑	Avoid in intracranial disease. Useful in fractious animals. Care in hypovolaemic patients	Dogs: 2–10 µg/kg IM Cats: 5–20 µg/kg IM
Opioids	Normal	↓ HR +/– ↓ BP	↓	↓	↓	Reduce the required dose of induction and maintenance agents. Reduce response to intubation and surgical stimulus	See *Table 102* and Chapter 30
Benzodiazepines	Normal	No direct vascular effects	↓	↓	↓↓	Possible sedative/anxiolytic. Reduce induction agent. Potentiate respiratory depression of other agents	Diazepam, 0.1–0.5 mg/kg IV; midazolam, 0.1–0.5 mg/kg IV or IM
Lidocaine	Normal	↓ BP: VD and ↓ CO	↓	↓	Low dose: ↓ High dose: ↑	Reduce response to intubation and extubation. Decrease seizures. Analgesia (see Chapter 30)	Co-induction: 1 mg/kg IV
Thiopentone	Normal	↓ BP: VD and ↓CO	↓↓	↓↓	↓	Excitement in unsedated animals. Accumulates with repeated dosing	Up to 10 mg/kg IV
Propofol	Normal	↓ BP: VD and ↓CO	↓↓	↓↓	↓	Excitement-free induction. Suitable for maintenance of anaesthesia in dogs with intracranial disease	Induction: up to 2–4 mg/kg IV. Maintenance: 0.2–0.4 mg/kg/minute
Ketamine	Normal	↑ HR and BP	↑↑	↑	↑	Avoid in animals with intracranial disease. Avoid in animals at risk of seizures (e.g. post myelography)	1–2 mg/kg IV

CBF = cerebral blood flow; CMR = cerebral metabolic rate; ICP = intracranial pressure; NR = not reported; BP = blood pressure; HR = heart rate; CO = cardiac putput; VD = vasodilatation; VC = vasoconstriction.

* *Note:* These dose rates are based on those used in normal animals and lower doses may be required in animals with CNS disease.

Table 101 **Co-induction agents for use in animals with central nervous system disease**

AGENT	DOSE* AND TIMING	COMMENTS
Butorphanol	0.1–0.2 mg/kg IV 1–2 minutes prior to induction	Potent antitussive. Mild analgesia only: avoid in surgical or animals in pain. Antagonize effects of mu agonists
Fentanyl	1–5 µg/kg IV 5 minutes prior to induction	Bolus administration can cause significant bradycardia. Exacerbates respiratory depression of induction agent. Capnography and appropriate manual or mechanical ventilation should be commenced. Also useful for reducing the autonomic response to endotracheal intubation
Diazepam or Midazolam	0.1–0.2 mg/kg IV immediately prior to induction	Negligible cardiovascular depression. Can cause disinhibition and paradoxical excitement: follow with induction agent immediately. May exacerbate respiratory depression of induction agent. Capnography and appropriate manual or mechanical ventilation should be commenced
Lidocaine	1–2 mg/kg IV 1–2 minutes prior to induction	DO NOT USE IN CATS. Can exacerbate cardiovascular depression of other agents. Also useful for reducing the autonomic response to endotracheal intubation

*Lower end of dose range is recommended in critically ill animals.

Table 102 **Opioids used intraoperatively to control pain and stabilize anaesthesia**

OPIOID	ADVANTAGES	DISADVANTAGES	COMMON DOSE RATES*
Fentanyl	Potent analgesia (full mu agonist). Short acting after bolus administration (15–20 minutes). Suitable for infusion	Marked respiratory depression at higher doses. Duration of action increases with duration of infusion	Bolus: 1–2 µg/kg IV q15–20 minutes. CRI: 0.2–0.7 µg/kg/min
Alfentanil	Potent analgesia (full mu agonist). Fast onset: 1 minute. Short duration after bolus administration (5 minutes). Suitable for infusion	Marked respiratory depression at doses used intraoperatively. Duration of action increases with duration of infusion	0.5–2 µg/kg/minute
Remifentanil	Potent analgesia (full mu agonist). Very short acting (1–2 minutes). Suitable for infusion. Duration of action is constant regardless of duration of infusion	Marked respiratory depression at doses used intraoperatively. Very rapid recovery: additional analgesia required before stopping infusion	0.2–0.7 µg/kg/minute

* Doses are a guide only and should be titrated on an individual patient basis.

Maintenance of anaesthesia

Following induction of anaesthesia it is essential to select drugs and apply techniques that will either decrease or minimally increase ICP.

Total intravenous anaesthesia

Total intravenous anaesthesia (TIVA) with suitable agents provides the best conditions for the maintenance of anaesthesia in the neurological patient, providing normocapnia ($P'ETCO_2$ 30–35 mmHg [4–4.7 kPa]) and systemic BP are maintained. TIVA can be achieved with variable rate infusions of propofol (0.2–0.4 mg/kg/minute) or target controlled infusion (TCI) of propofol (2.5–3.5 μg/ml of blood) using specialized infusion equipment. Propofol is frequently infused in combination with short-acting opioids (**409**) (see *Table 102*) to allow the dose of propofol and, therefore, its associated side-effects to be reduced. Additional information on TCI can be found in the Further reading list for this chapter.

The use of opioids (e.g. fentanyl (0.2–0.7 μg/kg/minute, remifentanil 0.2–0.7 μg/kg/minute) in combination with propofol allows the dose of propofol required for maintenance of anaesthesia and, in turn, the cardiovascular side-effects, to be reduced.

TIVA is the authors' preferred technique for canine neurosurgical patients and unstable patients requiring diagnostic imaging. The TIVA protocol utilizing propofol in cats is less well established and less commonly practised. Cats are inefficient metabolizers of propofol, predisposing to prolonged recoveries. Their RBCs are also more prone to the oxidative effects of the propofol (this may cause a Heinz body anaemia). Alfaxalone may prove to be a suitable alternative, as it has a similar pharmacokinetic profile to that of propofol, thus making it ideal for infusion. Infusion rates of alphaxalone currently used clinically in healthy animals range from 0.07–0.1 mg/kg/minute. However, appropriate dose rates for use in neurological patients have not been determined and the quality of recoveries in these patients is not known.

Inhalation anaesthesia

Inhalation anaesthesia can be used for short anaesthetics in stable neurological patients. It is preferred by many anaesthetists for maintenance of anaesthesia in cats given the concerns about using propofol by infusion. The characteristics of inhalation agents are summarized in *Table 103* (*next page*).



▲ **409** **Propofol can be administered by variable rate infusion where the rate is adjusted by the operator.**

Sevoflurane and isoflurane have the least effect on ICP providing the dose is minimized and the animals are ventilated to normocapnia. As described below, infusion of short-acting opioids is a useful technique for reducing the required dose of inhalation agent. Despite efforts to prevent herniation of the brain, there are still anecdotal reports of this life-threatening complication occurring when these agents are used to maintain anaesthesia during intracranial surgery in small animals. Other volatile agents, such as halothane, desflurane and N_2O, have a marked effect on ICP and are best avoided.

Maintain adequate ventilation and oxygenation

To maintain adequate ventilation and ensure normocapnia ($PaCO_2$ 35–40 mmHg [4.7–5.3 kPa]; $P'ETCO_2$ 30–35 mmHg [4–4.7 kPa]), the use of IPPV and measurement of end tidal CO_2 concentration breath by breath are essential.

To maintain oxygenation during diagnostic procedures and surgery it is not uncommon to use high inspired concentrations of oxygen during anaesthesia. For long-term ventilation the FiO_2 is ideally adjusted to the minimum required to maintain PaO_2 >80 mmHg (10.7 kPa) and minimize the risk of lung damage. In animals with concurrent pulmonary pathology, ventilation strategies employing PEEP may be required to maintain oxygenation. (For more details on IPPV and PEEP see Chapter 2.)

Table 103 **Inhalation agents for use in animals with central nervous system disease**

AGENT	CBF REGULATION	DIRECT CARDIOVASCULAR EFFECTS	CMR	ICP	SEIZURES	COMMENT
Halothane	Autoregulation: ↓↓ Flow-metabolism coupling: ↓ Chemical regulation: ↓	Cerebral VD ↓↓ MAP	↓	↑↑↑	None	Avoid in neurological patients
Isoflurane	Autoregulation: ↓ Flow-metabolism coupling: ↓ Chemical regulation: normal	Cerebral VD ↓↓ MAP	↓	↑	None	IPPV required. Rapid recovery. Use balanced anaesthesia to reduce dose and side-effects in neurological patients
Sevoflurane	Autoregulation: ↓ Flow-metabolism coupling: ↓ Chemical regulation: normal	Cerebral VD ↓↓ MAP	↓	↑	Reported in humans	IPPV required. Very rapid recovery. Use balanced anaesthesia to reduce dose and side-effects in neurological patients
Desflurane	Autoregulation ↓↓ Flow-metabolism coupling: ↓ Chemical regulation: normal	Cerebral VD ↓↓ MAP	↓	↑↑	None	IPPV required. Very rapid recovery. Use balanced anaesthesia to reduce dose and side-effects in neurological patients
Nitrous oxide	Not reported	Potent cerebral vasodilator. Minimal systemic effects	No effect	↑	None	Avoid in patients with increased ICP

CBF = cerebral blood flow; CMR = cerebral metabolic rate; ICP = intracranial pressure; VD = vasodilation; MAP = mean arterial pressure; IPPV = intermittent positive pressure ventilation.

Monitoring pulmonary function during anaesthesia is essential to ensure normocapnia ($PaCO_2$ 35–40 mmHg [4.7–5.3 kPa]) and adequate oxygenation (PaO_2 >80 mmHg [10.7 kPa]). For short anaesthetic procedures, such as for diagnostic imaging or CSF sampling, capnography and pulse oximetry are adequate for monitoring ventilation and oxygenation. For unstable patients or animals undergoing long procedures, such as surgery, analysis of serial arterial blood gas samples is essential. (For details on monitoring techniques, see Chapter 2.)

Maintain perfusion and cerebral perfusion pressure

To maintain CPP in patients with increased ICP, it is recommended that mean BP is maintained between 70 and 80 mmHg and systolic BP above 100 mmHg. For short procedures in stable patients undergoing MRI or CT, non-invasive BP monitoring is adequate. For unstable patients or for monitoring during surgical procedures, invasive, direct monitoring of arterial BP and CVP is preferred. (For details on BP and CVP monitoring see Chapter 2.)

Reduce cardiovascular depression associated with maintenance agents

As most anaesthetic agents cause dose-dependent decreases in BP, it is preferable to combine short-acting anaesthetic agents that can be titrated to effect with short-acting opioids that cause minimal cardiovascular depression. This will reduce the required dose of the selected maintenance agent in a dose-dependent fashion. The doses of opioids commonly used for maintenance of anaesthesia are provided in *Table 102*. Animals with severe neurological impairment may require lower doses.

An expected side-effect of administration of these potent opioids is respiratory depression. Even at low doses, significant hypoventilation may occur and IPPV may be required to maintain normocapnia. Both alfentanil and fentanyl will accumulate after a period of infusion, so it may be prudent to terminate or reduce the infusion rate prior to the end of anaesthesia to ensure adequate ventilation on recovery. Remifentanil does not accumulate and has a duration of action of approximately 3 minutes regardless of the duration of infusion.

Maintenance of normal fluid balance

Providing animals have normal fluid and electrolyte balance prior to anaesthesia, fluid therapy during anaesthesia initially consists of isotonic, polyionic crystalloids administered at 10 ml/kg/hour. Subsequent infusion rates and types of fluid will depend on losses and cardiovascular performance during anaesthesia. Measurement of CVP, arterial BP and urine output (UOP) is the best way to assess the response to fluid therapy. (For details on selection of fluids and rates for varying conditions see Chapter 31; for details of techniques for monitoring of BP, CVP and UOP see Chapter 2.)

Avoid sudden/marked increases in blood pressure

Various stimuli during anaesthesia, including nociception from surgical stimulation, can cause increases in BP, which in a diseased brain may result in an increase in CBF and ICP. To minimize sudden or marked increases in BP during anaesthesia, the continuous infusion of an opioid (as described above) can help minimize this sympathetic stimulation and the haemodynamic responses to surgery. This in turn will contribute to the maintenance of stable BP and CBF.

Maintain venous drainage from the head

Diagnostic imaging procedures and craniectomy are invariably performed with the patient positioned in sternal recumbency with the head level with the spine (**410**). This position is excellent for ensuring adequate lung expansion and also encourages venous drainage from the head. However, it is important to ensure that the jugular veins are not occluded when the animal is placed in this position, as this will lead to venous congestion within the brain and marked increase in ICP. For animals in lateral recumbency, mild head elevation (15–30 degrees) is also recommended to encourage cerebral venous drainage.

Measurement of CVP is generally performed via a catheter inserted into the jugular vein. This may increase the risk of disturbance to venous return and increased ICP. Methods for reducing the interference with venous return are described in Chapter 2.

The use of IPPV may also impede venous return from the head during the inspiratory phase of ventilation. To minimize this adverse effect, the inflation pressures required to maintain normocapnia can be reduced by administration of NM blockade using drugs such as atracurium. Atracurium is initially administered at 0.2–0.5 mg/kg IV. This is followed by increments of 0.1 mg/kg, which is administered according to NM activity assessed using a nerve stimulator.



▲ **410** In animals with intracranial disease, venous drainage from the head is maintained by positioning in sternal recumbency with the head at the same level as the spine.

Maintain body temperature

Body temperature should be maintained as close to normal as possible. Hypothermia has numerous adverse effects on the patient including:

- Cardiovascular system depression with bradycardia and hypotension.
- Suppression of the immune system and an increased risk of infection.
- Delayed healing.
- Intra- and postoperative coagulopathy and increased blood loss.
- Slow recovery.
- Shivering on recovery, which increases oxygen demand when oxygen delivery may be compromised.
- Prolonged hospital stays.

Hyperthermia, on the other hand, increases CMR, which increases CBF and can lead to increases in ICP and further reductions in CPP.



▲ **411** **Following brain surgery, animals should be recovered in a controlled, quiet manner. Extubation is a balance between ensuring normal ventilation and preventing coughing when the endotracheal tube is removed.**

It is important to remember that head trauma (especially if it involves the hypothalamus) can result in impaired thermoregulation. Close monitoring of the temperature in these animals is imperative and appropriate therapy should be initiated when abnormalities arise. Methods for maintaining normal body temperature in animals with neurological disease will be discussed in more detail in the NM disease section below.

Recovery from anaesthesia

The aims during the recovery period are to achieve a smooth emergence from anaesthesia with minimal excitement, coughing or straining, and adequate ventilation (**411**). The timing of extubation is a compromise between ensuring the animal can protect its own airway, breathe spontaneously and maintain normocapnia, while avoiding stimulation that can lead to increases in arterial BP and coughing.

Ensure adequate ventilation

Reduce rates of opioid infusions

If high infusion rates of opioids have been used during surgery, it is important that the infusion rate is reduced in preparation for recovery. Once the patient is extubated and IPPV can no longer be delivered, it is imperative that the patient can breathe spontaneously. Extubation should therefore only be performed when the patient can spontaneously ventilate adequately (check the capnograph or blood gases).

When using either an alfentanil or fentanyl infusion, the rate should be reduced approximately 30 minutes prior to extubation. This will depend to some extent on the duration of infusion and the total amount of drug that has been delivered (the higher the dose and the longer the infusion, the more time required to reduce serum concentrations).

Remifentanil does not accumulate and activity rapidly disappears after infusion is stopped, allowing prompt return to spontaneous ventilation. The disadvantage is that the analgesic activity is also rapidly terminated. If continued analgesia is required, another opioid must be administered prior to turning off the remifentanil infusion. This may be in the form of a long-acting opioid such as methadone. Alternatively, infusion of short-acting opioids at a lower dose (see Chapter 30) can be used to provide postoperative analgesia so long as the patient can breathe spontaneously.

Assess adequacy of spontaneous ventilation periodically

When preparing to extubate, the ETT tie is undone and the cuff left inflated. As the depth of anaesthesia decreases, trial periods of apnoea are performed. If spontaneous ventilation and maintenance of normocapnia occur, then the animal can be extubated; otherwise IPPV is reintroduced before $P'ETCO_2$ exceeds 45 mmHg. Once extubated, the patency of the airway needs to be assessed, particularly in animals with brachycephalic airway syndrome. It is important to have ready access to an induction agent in case immediate reintubation is required.

Minimizing coughing and hypertension on recovery

To minimize laryngeal stimulation, the administration of agents such as fentanyl or lidocaine can be used as described for intubation. At the end of anaesthesia, the drugs are given just prior to expected extubation. Alternatively, in animals requiring ongoing analgesia, a continuous infusion of fentanyl (2–5 μg/kg/minute) can also help reduce coughing on extubation.

Hypertension in the recovery period despite adequate analgesia can be treated by administration of β receptor antagonists or blockers (e.g. esmolol, 50–200 μg/kg/minute CRI). More details on hypertension in neurological patients can be found in Chapter 2.

Minimizing agitation in the perianaesthetic period

Agitation is not uncommon in animals with intracranial disease. Administration of opioid analgesics will ensure the agitation is not caused by pain. If it persists, then sedative agents such as acepromazine or dexmedetomidine will be required, but as these agents have adverse effects on the CNS and the cardiovascular system, their benefits for controlling agitation and calming the patient need to be weighed against the adverse effects that may occur. If administration of these agents is deemed necessary, low doses should be used and blood volume and BP should be normalized before administration. For example, the authors have used acepromazine (5–10 μg/kg IM) to control agitation in dogs post craniectomy when other methods of controlling the agitation have failed and the animal is considered at risk of injury from the agitation. Trazodone hydrochloride, a triazolopyridine derivate and member of the phenylpiperazine class of drugs, can also be considered as an anxiolytic in these situations (see Further reading).

SPINAL DISEASE

Considerations

Anaesthesia in animals with spinal disease should be designed to maintain spinal perfusion and minimize further neurological injury. As a result, many of the principles of anaesthesia for patients with intracranial disease are relevant to patients with spinal disease. Considerations for anaesthetizing animals with spinal disease are outlined in *Table 104* (*next page*).

Stabilization

Animals with spinal trauma frequently have other injuries. Patients with spinal disease may have had reduced access to water due to reduced mobility (**412**). Stabilization of pulmonary and cardiovascular functions and correction of fluid and electrolyte deficits should be performed prior to anaesthesia. A full clinical examination should be performed with particular attention paid to the function of the cardiovascular and respiratory systems.



▲ **412** Spinal patients may have reduced access to water due to immobility. This may predispose to dehydration if supplemental fluid is not provided. Dogs, such as the one in this photograph, will need to be administered fluids intravenously or frequently 'by hand'.

Table 104 **Considerations for anaesthetizing animals with spinal disease**

CONSIDERATION	MANAGEMENT
Maintain perfusion	Correct deficits in circulating blood volume and body water. Use agents/techniques that minimally depress cardiovascular function
Pain	Most spinal diseases are painful and effective analgesia (e.g. full mu agonists) is necessary
Anxiety	Anxiety is common in paralysed animals and decreases the pain threshold. Administering anxiolytics is an important part of pain management in spinal patients
Mechanical instability	Animals need to be moved carefully to minimize further trauma to the spinal cord, particularly when a fracture or luxation is suspected. Intubation of animals with suspected instability of the cervical spine should also be performed carefully. Flexion and extension of the head should be avoided
Respiratory insufficiency	Cervical spinal lesions can interfere with innervation of the diaphragm and intercostal muscles, leading to inadequate ventilation and respiratory arrest. Sternal recumbency during surgery restricts movement of the diaphragm and thus mechanical ventilation is recommended during surgery to ensure adequate ventilation
Maintain airway	Ventral approaches to the cervical spine require retraction of the trachea and may partially or completely obstruct the endotracheal tube
Blood loss	Blood loss during surgery can be significant and needs to be monitored closely by weighing swabs and measuring fluid in suction bottles. Transfusion is indicated if >20% of circulating blood volume is lost or if signs of hypovolaemia (increased heart rate without increased MAP, pale mucous membranes) are observed

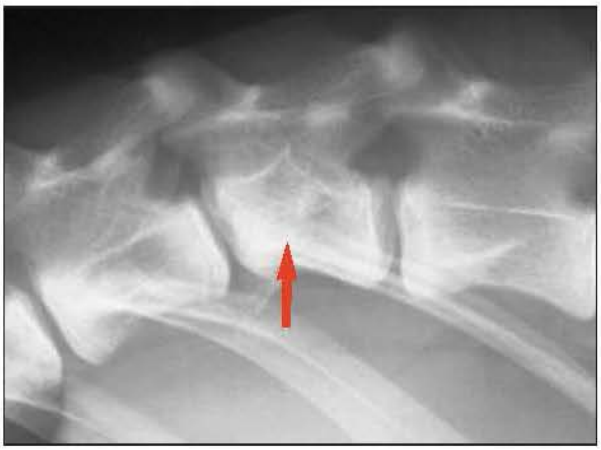
Guidelines for sedating and anaesthetizing animals with spinal disease

Premedication

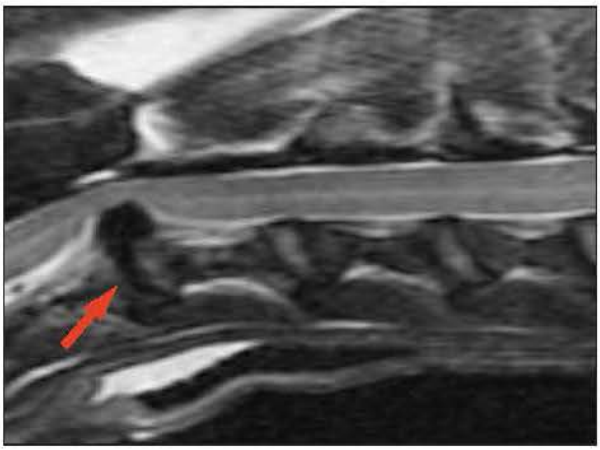
Premedication is important not only to provide analgesia and minimize the dose of induction agent required, but also to increase the ease of handling without the need for excessive physical restraint, which may be dangerous for these patients.

Choosing drugs and drug combinations

Opioids form the basis for premedication of animals with spinal disease and are generally administered on their own to patients with other systemic abnormalities. A variety of other agents can be used in conjunction with opioids to provide additional sedation if required. The doses and advantages and disadvantages of these agents are outlined in *Table 101*. Acepromazine is useful in anxious but otherwise stable animals. Medetomidine can be used in extremely anxious or fractious animals that are normally hydrated and cardiovascularly stable. Benzodiazepines are unpredictable and unreliable sedatives in healthy dogs and cats, but may provide useful sedation in critically ill animals. Medetomidine and benzodiazepines both cause skeletal muscle relaxation and should be avoided in animals with unstable spinal fractures (**413**). Ketamine is another option in normovolaemic cats with normal renal function in combination with opioids, acepromazine or benzodiazepines. However, ketamine is extremely painful when injected intramuscularly. This may cause additional discomfort to animals already in pain. In addition, sudden uncontrolled movement in response to the injection may be detrimental in animals with an unstable spinal fracture.



▲ 413 Handling and choice of premedication should be performed carefully in animals with unstable spinal fractures, such as that noted on this lateral thoracolumbar radiograph (arrow).

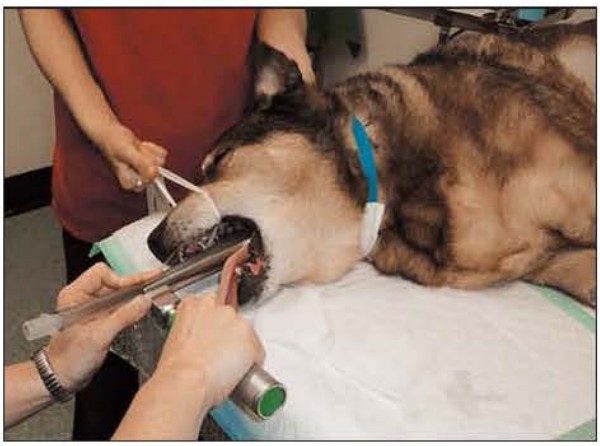


▲ 414 For animals with cranial spinal lesions, such as the C2/C3 disc extrusion seen on this sagittal MR image (arrow), intubation should be performed with support of the head and neck.

Induction

Minimize further damage to spinal cord

A rapid and controlled induction of anaesthesia with minimal struggling is best achieved with intravenous agents. Endotracheal intubation should be performed carefully with adequate support of the head and neck, particularly in animals with cervical spinal cord injury (**414**). Intubation is facilitated by the use of a laryngoscope (**415**). Excessive extension of the neck should be avoided in dogs with caudal cervical lesions, while excessive flexion should be avoided in animals with AA subluxation or other cervical fractures.



▲ 415 Intubation is best performed with the animal in lateral recumbency. Use of a laryngoscope will aid visualization of larynx.

Select induction agents that minimally interfere with spinal perfusion

Selection of an appropriate induction agent is based on the same basic principles as those described for animals with intracranial disease. The characteristics of the intravenous agents and suggested doses are described in *Table 100*. To decrease the required dose of intravenous induction agent and to minimize cardiovascular depression, concurrent administration of a potent opioid, such as fentanyl or a benzodiazepine, can be used during induction (*Tables 101* and *102*).

Maintenance of anaesthesia

Select agents that maintain spinal perfusion

Maintenance of anaesthesia is usually performed with inhalation agents. As autoregulation of perfusion to the spinal cord and chemoreceptor response to carbon dioxide are better maintained with isoflurane and sevoflurane than halothane, these are the preferred inhalation agents. Nitrous oxide is reported to increase ICP as a result of cerebral vasodilation, so is best avoided in patients with intracranial disease. Whether the same precautions are warranted in animals with spinal cord injury and compression is not known.

Infusion of short-acting opioids can also be used in conjunction with inhalation agents. These agents provide analgesia, which is essential in most animals with spinal disease, and will help reduce the dose and thus the amount of cardiovascular depression observed with inhalation agents. Details of the use of these opioids are described in the section on intracranial disease.

Maintenance of anaesthesia can also be performed with a TIVA technique as described for intracranial disease. TIVA is especially useful for dogs requiring surgery of the cranial cervical spinal cord where manipulation of the cervical spinal cord and/or brainstem may occur (e.g. repair of AA instability).

Maintain adequate ventilation

IPPV is recommended during anaesthesia in spinal patients for several reasons. Firstly, the detrimental effects of inhalation agents on spinal blood flow regulation can be minimized by maintaining normocapnia. Secondly, surgical access frequently requires that the animal is positioned in sternal recumbency, which can interfere with diaphragmatic excursions and impair ventilation. Finally, the dose rates of the opioid agonists recommended for intraoperative use produce marked respiratory depression and therefore necessitate IPPV.

Maintain adequate perfusion

Intravenous fluid therapy is essential during anaesthesia in all spinal cases to maintain fluid balance, adequate BP and perfusion of the spinal cord. In hypovolaemic animals, the volume deficit should be replaced before anaesthesia. Intraoperative blood loss can be unpredictable and surprisingly high during spinal surgery. Blood loss should be estimated regularly by counting blood-soaked swabs, weighing swabs (1 ml of blood weighs approximately 1.03 g) or measuring the volume of fluid in suction bottles (taking into account dilution from irrigation fluids).



▲ 416 **Heat and moisture exchange devices can be placed between the endotracheal tube and the breathing circuit to help reduce heat and moisture loss from animal.**

Blood loss can also be estimated from the PCV of fluid in the suction bottle. This technique requires an accurate measurement of the patient's PCV at the time of blood loss. The PCV prior to anaesthesia may not be representative of the PCV during anaesthesia. The PCV may decrease due to splenic sequestration of RBCs in response to anaesthetic agents (propofol, barbiturates) and dilution by intravenous fluid therapy. If an accurate estimate of the PCV of the patient prior to haemorrhage is known, the amount of blood in the bottle can be estimated using the following:

$$\text{Amount of blood lost (ml)} = \frac{\text{PCV of flush in bottle} \times \text{total volume of fluid in bottle}}{\text{PCV of patient at time of haemorrhage}}$$

A blood transfusion is indicated when blood loss exceeds 20% of the circulating blood volume or haemoglobin concentration is <80 g/l (<8 g/dl). Blood loss of less than 20% can be managed by administrating crystalloids +/– colloids such as hetastarch (maximum dose 20 ml/kg/day). (For more details on fluid therapy see Chapter 31.)

Maintain body temperature

Heat loss can be a problem, particularly when spinal cord injury causes sympathetic nervous system imbalance and peripheral vasodilation. Monitoring core body temperature should be performed during anaesthesia. Heat loss can be prevented during anaesthesia by heat pads, warm water beds or warm air blowers and 'blankets'. Heat and moisture exchange devices (**416**) can be placed between the endotracheal tube and the breathing system to promote warmth and humidification of inspired gases.

Monitoring

During diagnostic imaging and surgery in animals with spinal disease, non-invasive monitoring of cardiopulmonary function with electrocardiography, non-invasive BP measurement, capnography and pulse oximetry is generally adequate. In animals where cardiopulmonary dysfunction (e.g. cranial cervical surgery, trauma involving multiple organ systems) or excessive blood loss is expected, invasive BP measurement is recommended. Monitoring techniques have been discussed in detail in Chapter 2.

Recovery

It is essential that the provision of analgesia is continued into the postoperative period to ensure a calm and comfortable recovery. In some cases the use of low-dose sedatives, such as acepromazine (0.01–0.02 mg/kg IM or IV) or dexmedetomidine (0.5–1.0 µg/kg IV bolus or infusion of 0.5–1.0 µg/kg/hour), may be required in extremely stressed or agitated animals exhibiting signs of suboptimal emergence. However, these drugs should only be used in animals with normal cardiovascular function. Trazodone (see p. 545) can also be used to treat postoperative anxiety. (For details on possible postoperative analgesia see Chapter 30.)

NEUROMUSCULAR DISEASE

Considerations

Considerations for anaesthetizing animals with NM disease are outlined in *Table 105*. The general principles for anaesthetizing these patients are similar, with some differences depending on the type of NM disease present. These principles are described in more detail in regard to premedication, induction, maintenance and recovery of anaesthesia.

Stabilization

Fluid and electrolyte abnormalities are common in these patients due to immobility and an inability to eat and drink. These deficits need to be corrected prior to anaesthesia when possible. Fluid and acid–base abnormalities associated with toxicities, such as metaldehyde, will also need to be corrected prior to anaesthesia (see Chapter 28).

Animals with aspiration pneumonia should be stabilized as much as possible prior to anaesthesia. Antibiotic and oxygen therapy forms the basis of symptomatic treatment in these animals.

Premedication

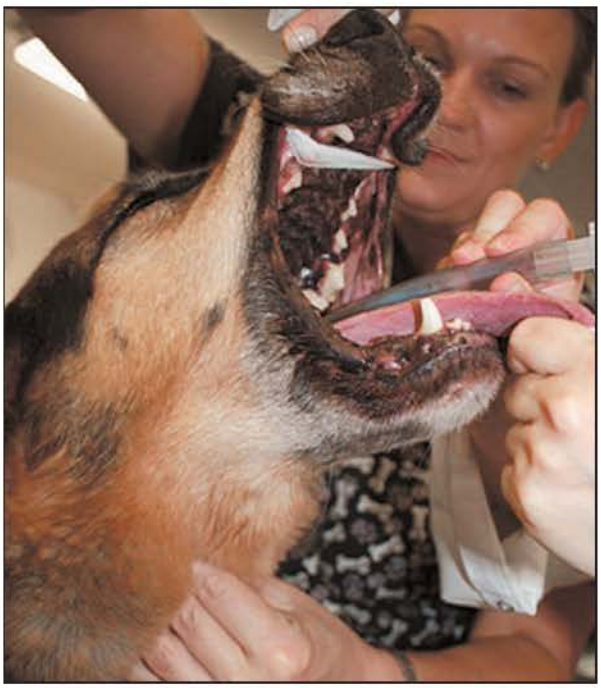
The use of premedication in animals with peripheral NM disease will depend on the type of disease that is present, how painful that disease is and how urgent the need for anaesthesia is (e.g. an animal with airway obstruction requires immediate anaesthesia). In anxious animals, the judicious use of sedatives may be needed to facilitate a smooth, stress-free induction. (*Note:* Sedation can interfere with the maintenance of a patent airway and increase the risk of upper respiratory tract obstruction and aspiration. If used, low doses are recommended and animals should be constantly monitored for any adverse effects.)

In animals with painful NM disease (which is uncommon), premedication should include an opioid, either alone or in combination with other agents. Opioid premedicants should also be given to animals requiring muscle and nerve biopsies and animals undergoing painful diagnostics such as electromyography.

Induction of anaesthesia

Maintain oxygenation

The patient should be pre-oxygenated for 5–10 minutes prior to induction when possible. If an animal objects to the placement of a face mask, the use of flow-by oxygen is recommended. Flow-by oxygen is preferred in animals predisposed to hyperthermia, because masks encourage re-breathing of warm expired gases. Pre-oxygenation increases the concentration of oxygen in the functional residual capacity of the lung and delays the onset of hypoxaemia in the event of a difficult intubation or in patients with cardiovascular or respiratory compromise.



▲ **417** Animals that are at risk of regurgitation during induction should be maintained in sternal recumbency with cricoid pressure applied until the endotracheal tube is placed and cuff inflated.

Prevent regurgitation and aspiration

Induction of anaesthesia should be performed with the patient in sternal recumbency (**417**). If there is an increased risk of regurgitation (e.g. megaoesophagus), cricoid pressure should be applied. Cricoid pressure is maintained until the ETT is placed and secured in the airway with the cuff inflated. Suctioning of the pharynx, oesophagus and stomach should be performed as soon as the airway is secure to minimize the risk of aspiration during anaesthesia (if the cuff becomes deflated). If vomiting or regurgitation occurs during induction of anaesthesia and before the airway is protected by the presence of an ETT, the animal should immediately be positioned with its head over the edge of the table to allow gravity-assisted drainage of the pharynx. The pharynx and oesophagus should be suctioned before intubation is performed.

Induction of anaesthesia should be performed with short-acting intravenous agents that facilitate rapid control of the airway. Furthermore, a prompt recovery from anaesthesia is important in order for the patient to regain control of its airway as soon as possible. Agents such as propofol and alfaxolone allow rapid recovery; however, in animals at risk of obstruction, titration of these agents to effect can delay intubation. Furthermore, bolus administration can lead to marked decreases in BP. To reduce the dose and thus the side-effects, co-induction agents (fentanyl + short-acting benzodiazepines) can be administered immediately prior to an intravenous induction agent. This combination of agents will invariably cause apnoea and therefore animals should be ventilated as soon as intubation is performed. Ketamine should be avoided in animals with tetanus and increased muscle activity. Thiopentone allows rapid control of the airway, but the recovery period is likely to be prolonged.

Maintenance of anaesthesia

Selection of agent

Agents with a short duration of action, thus allowing rapid recovery, are preferred. Inhalation agents, such as isoflurane, sevoflurane and desflurane, all have physicochemical properties that ensure a rapid clinical response to changes in vapourizer settings. In addition, recovery from anaesthesia is relatively rapid, with prompt return of airway reflexes.

Table 105 **Considerations for anaesthetizing animals with neuromuscular disease**

CONCERN	CONSIDERATIONS
Pain	Presence and severity of pain will vary with the disease. Painful conditions include polyradiculoneuritis, some myopathies and muscle and nerve biopsy patients
Dysphagia	Weakness of pharyngeal muscles results in difficulty swallowing and predisposes to aspiration
Airway obstruction	Laryngeal paresis or paralysis. Laryngeal spasm (e.g. tetanus)
Impaired ventilation	Mechanical ventilation frequently required due to: • Weakness of respiratory muscles (e.g. snake envenomation, myasthenia gravis, polyradiculoneuritis, tetrodotoxin, botulism). • Spasm of diaphragm and intercostals (e.g. tetanus)
Impaired oxygenation	Dysphagia, megaoesophagus and inability to protect the airway predisposes to aspiration. Recumbency predisposes to atelectasis. Supplemental oxygen recommended in peri-operative period
Impaired thermoregulation	Laryngeal dysfunction and impaired ventilation reduce ability to pant and predispose to hyperthermia during exposure to warm environments. Muscle fasciculations and tetany increase metabolic rate and predispose to hyperthermia. Generalized weakness prevents shivering and predisposes to hypothermia during exposure to cold environments
Dehydration and electrolyte abnormalities	Recumbent animals may have restricted access to water. Dysphagia impedes ability to eat and drink. Regurgitation associated with megaoesophagus increases loss of water and bicarbonate (from saliva)

Ensure adequate ventilation

Mechanical ventilation is recommended in all animals with peripheral NM disease as there is likely to be a component of respiratory muscle involvement. IPPV should be delivered with close monitoring of CO_2 concentration in the expired gas with a capnograph or serial arterial blood gas analyses. Monitoring of the haemodynamic consequences of ventilation is also prudent.

Maintain normal body temperature

Animals with NM disease may have difficulty maintaining normal body temperature (see *Table 105*). It is therefore essential to monitor core body temperature perioperatively in these animals. Mild decreases in body temperature can be managed with passive warming (e.g. warm air blankets or warm water beds). It is easier to prevent hypothermia than to treat it, so all efforts to preserve body temperature should be made. Although it is unusual for animals to develop hyperthermia under anaesthesia, increases in body temperature should be managed by passive cooling.

Neuromuscular relaxation

In animals with peripheral NM disease requiring surgery for other reasons (e.g. thoracotomy for thymoma removal in animals with MG), NM relaxation may be required to improve surgical access. Non-depolarizing muscle relaxants can be used, but extreme care is required as prolonged duration of skeletal muscle weakness can occur. Depolarizing muscle relaxants such as suxamethonium should be avoided.

Non-depolarizing NM blocking agents should be administered in incremental doses with careful monitoring of peripheral nerve blockade with a nerve stimulator. There must also be facilities to provide either mechanical or manual IPPV and assessment of adequacy of ventilation (capnography or blood gas analysis). Shorter-acting NM blocking agents, such as atracurium or vecuronium, administered at one tenth of the usual dose, are the preferred agents. Infusions allow more precise control of the degree of NM blockade than boluses, which create peaks and troughs in plasma concentration and thus cause relative overdose and relative underdose, respectively.

Recovery

Maintain adequate oxygenation and ventilation

As the animal recovers from anaesthesia, it is essential to monitor end-tidal CO_2 to ensure spontaneous ventilation is sufficient to maintain normocapnia. These animals will invariably have some degree of pulmonary pathology due to aspiration or atelectasis, so oxygenation should be monitored throughout recovery and supplemental oxygen provided until the animal can maintain SpO_2 >95% when breathing room air. Initially, this can be performed via the ETT; however, following extubation, oxygen can be provided by mask, oxygen cage or nasal catheters. Where oxygenation is expected to be poor for prolonged periods (e.g. animals with pneumonia or animals expected to be recumbent following anaesthesia), nasal catheters should be placed before the end of anaesthesia to provide a smooth stress-free transition from oxygenation via the ETT to the nasopharyngeal catheters. (*Note:* Animals that develop upper respiratory tract obstruction [e.g. laryngeal paralysis or laryngeal spasm] following extubation may require a tracheostomy to maintain adequate oxygenation and ventilation [see below].)

Prevent aspiration

Suctioning of the oesophagus and pharynx should be performed prior to recovery in order to minimize the risk of regurgitation at extubation. The animal is best positioned in sternal recumbency with the head elevated to maximize chest excursions and respiratory function. In addition, elevation of the head will help prevent passive regurgitation. Should vomiting or regurgitation occur during recovery, the animal's head must be positioned over the edge of the table to allow fluid or stomach contents to flow out of the mouth. If the animal is still sufficiently anaesthetized, the pharynx and mouth can be cleared by suctioning and swabbing. To prevent oesophagitis associated with regurgitation of gastric contents, the oesophagus should ideally be carefully lavaged until the fluid retrieved is clear. It is essential that the ETT is secured in place with adequate cuff inflation when lavage is performed.

Maintain a patent airway

Animals with neuromuscular weakness or post-gastric lavage

In these animals extubation is delayed for as long as possible to ensure upper and lower respiratory muscle function is adequate. Recovery should be performed in a quiet, dimly lit environment to minimize stimulation on recovery. The cuff of the ETT=endotracheal tube is left inflated until the animal is ready to be extubated. Adequate analgesia must always be provided in animals with painful diseases to optimize conditions for a smooth emergence from anaesthesia. Low-dose infusions of short-acting opioids can also help reduce stimulation from the ETT and help maintain a patent airway for longer.

Animals with tetanus

Although tetanus does not cause NM pathology, it is associated with severe muscle spasms. Extubation in patients with tetanus can stimulate laryngospasm. The safest approach is to recover these animals with a tracheostomy in place. If a tracheostomy is not performed, laryngospasm can be minimized by extubating early, as long as the patient is ventilating spontaneously. Topical lidocaine applied to the larynx may also help. In any case, it is essential to be prepared to perform an emergency tracheostomy should laryngospam occur and if reintubation is too difficult. Preparing the site beforehand is recommended to save time should a tracheostomy be required. The ability to provide oxygen supplementation via an intratracheal needle or catheter should also be available in case upper respiratory tract obstruction occurs (see Chapter 2). (*Note:* This method of providing oxygen is only suitable for short periods, as there is no concurrent ventilation, and overinflation of the lungs can occur because there is no outflow for the insufflated oxygen.)

Table 106 **Possible agents for sedating or anaesthetizing animals during long-term ventilation**

DRUG	DOSE	COMMENTS
Inhalation agents: isoflurane/sevoflurane	1 minimum alveolar concentration equivalent or less	Not recommended for long-term ventilation in animals with intracranial disease. Isoflurane can be irritant to airway and therefore is best avoided. May have adverse effects in airway disease or prolonged anaesthesia
Propofol	0.05–0.4 mg/kg/minute	Ideal for animals with intracranial disease. Can be used for any animal requiring sedation or anaesthesia for ventilation
Midazolam	0.05–0.2 mg/kg/hour (do not dilute drug with Hartmann's)	Can be used in animals with intracranial disease that require sedation for intubation. Dysphoria observed with prolonged infusion may cause stressful recoveries. Use cautiously in animals with neuromuscular weakness
Fentanyl	0.2–0.7 µg/kg/minute	Can be used alone in paralysed animals or in conjunction with other agents to provide analgesia/sedation

SEDATION/ANAESTHESIA FOR CHRONIC INTUBATION AND MECHANICAL VENTILATION

The choice of agent used to maintain anaesthesia in animals requiring ventilation will depend on the indications for ventilation, the expected duration of ventilation and whether the animal has an oral ETT or a tracheostomy. Ventilation techniques are discussed in Chapter 2. Examples of agents that can be used to provide sedation or anaesthesia for ventilation are listed in *Table 106*.

Dose rates

Maintenance of anaesthesia has 'lighter' requirements than does surgical anaesthesia, and in some cases sedation only may be needed. In animals intubated via tracheostomy, the depth of sedation/anaesthesia will be even lower, as the stimulus associated with oral intubation is absent. Animals that are weak, paralysed or suffering from CNS depression will also require much lower doses than those with normal CNS activity. Therefore, short-acting agents that can be titrated to achieve the required level of sedation or anaesthesia in each individual are preferred.

Additional considerations for paralysed animals

The use of sedation or anaesthesia for ventilating paralysed animals warrants special mention. Sedation or anaesthesia is not required to tolerate the presence of an ETT; however, as they recover from paralysis, sedation or anaesthesia will be required to maintain intubation. The reason for this is the differential recovery of different skeletal muscles from paralysis, allowing these animals to move before being able adequately to ventilate or protect their own airway. As a result, these animals can start to struggle. Furthermore, it must be remembered that even when a patient is fully paralysed they are conscious and responsive to their environment, therefore some sedation and/or analgesia is required to minimize stress and discomfort.

Nursing and airway management of the chronically ventilated patient are covered in Chapter 2.

SPECIFIC CONSIDERATIONS FOR DIAGNOSTIC PROCEDURES

Myelography

Myelography is associated with a risk of seizures on recovery from anaesthesia and a variety of cardiopulmonary abnormalities that can occur during anaesthesia, particularly during/after contrast injection (**418**).

Seizure activity

Seizure activity is a recognized adverse effect of injection of contrast agents into the subarachnoid space. The risk of seizures is influenced by several factors including the volume and rate of contrast injection, the site of injection, the size of the animal, duration of anaesthesia after injection and the position of the animal during injection. Seizures are more commonly observed after CMC myelography compared with lumbar myelography. Animals weighing >20 kg are also observed to have a higher incidence of seizures, possibly due to the relatively higher volume of contrast injected.

To reduce the risk of seizures, the dose rate should be calculated from surface area rather than body weight, the speed of injection should be slow and the head should be elevated as soon as injection is complete to promote the flow of contrast away from the head. The use of a tilting table allows head elevation while keeping the animal's spine straight and supported.

Pharmacological agents that decrease the seizure threshold should be avoided. Acepromazine, ketamine and medetomidine have been previously reported to decrease the seizure threshold, and most of the literature recommends that these agents are not used in animals undergoing myelography. However, the association between use of acepromazine and seizure activity has become increasingly unclear and its effect may depend on the cause of the seizure activity. The authors recommend that its use be avoided whenever possible and if required for sedation/anxiolysis, it is used carefully and at low doses.

Seizures have been reported to occur up to 6 hours after contrast injection, so these animals should be closely monitored during this time. If seizures occur, administration of diazepam (0.2–1.0 mg/kg IV) is recommended as the first-line treatment.



▲ **418** **Myelography is frequently performed to diagnose intervertebral disc disease (as seen here). Performance of a myelogram requires special considerations for anaesthesia. (Photo courtesy Victoria Johnson)**

Cardiopulmonary disturbance

Cardiopulmonary side-effects during or immediately after the injection of contrast have been observed and include apnoea, tachypnoea, bradycardia, tachycardia, arrhythmias, hypotension and hypertension. Many of these effects are associated with the discomfort or pain of injection and can be minimized by slowing the injection rate and ensuring an adequate depth of anaesthesia during injection. Transient increases in ICP may also be responsible, particularly with cisternal contrast injections. Careful monitoring of cardiopulmonary function is necessary during myelography to detect any problems early and treat accordingly.

Magnetic resonance imaging

The main considerations for anaesthetizing patients with intracranial and spinal disease for MRI are described in the relevant sections earlier in this chapter. In addition, there are several important considerations unique to anaesthetizing a patient within a magnetic field.

Equipment hazards

Ferromagnetic objects can become dangerous projectiles and may result in injury and/or death to the patient or personnel within the scanning room. It is essential that these objects remain outside the 5 gauss line. Anaesthetic machines are required to be as close to the patient as possible to minimize the length of the breathing system and should be composed of non-ferromagnetic materials. If this is not possible, a non-rebreathing anaesthetic circuit (e.g. Bain) can be used, as the length of the inspiratory and expiratory tubes (which are coaxial) may be effectively infinite. Non-ferromagnetic objects within a magnetic field (e.g. ECG leads) have the potential to induce electric currents, leading to heating and burns. The risk of burns can be minimized by insulating the wires, separating the wires from the skin by padding, avoiding large loops of wire that allow the induction of currents and applying sensors as far away from the imaged area as possible.

Monitoring

Monitoring of the anaesthetized patient during MRI has inherent limitations. Equipment used for monitoring must be MRI safe and ideally MRI compatible. Equipment that is MRI safe has been demonstrated to present no additional risk to the patient. Equipment that is MRI compatible has been demonstrated to be both MRI safe and to not reduce significantly the diagnostic quality of the imaging procedure nor have its operation affected by the scanning procedure. MRI compatible equipment is currently available that allows distant monitoring of animals during MRI. Where cost is limited, some monitoring equipment, such as capnography, oesophageal stethosope and oscillometric methods of non-invasive BP measurement, can be used if the electrical components are outside the 5 gauss line.

Cerebrospinal fluid collection

The collection of CSF may be performed by CMC or lumbar puncture. CMC puncture requires flexion of the neck, which can cause inadvertent kinking of the ETT and respiratory obstruction. In addition, flexion of the neck can obstruct jugular veins, impair venous drainage and contribute to increased ICP. IPPV is essential during CMC puncture to ensure adequate ventilation and normocapnia.

ETTs reinforced with coiled wire resist kinking and can be used to prevent airway obstruction when the neck is flexed for collection of CSF. As these tubes contain metal, they are not suitable for use in animals undergoing concurrent MRI imaging.

In animals with increased ICP the collection of CSF carries the risk of parenchymal herniation. When sampling is essential for the diagnosis and treatment of the animal, pre-emptive use of mannitol (30 minutes prior to CSF collection) and reduction of $PaCO_2$ to 30 mmHg (4 kPa) by hyperventilation during the sampling period may reduce the risk of herniation.

Electroencephalography

Electroencephalography records the spontaneous electrical activity within the brain and may be performed in animals to identify areas of abnormal electrical activity responsible for seizures. Performance of electroencephalography in conscious animals is difficult, as muscle movement causes artefacts, which affect the diagnostic quality. Inhalational and intravenous anaesthetic agents also alter the electrical activity within the brain in a dose-dependent manner, thus limiting the amount of useful information that can be obtained from electroencephalography in anaesthetized animals. A sedative regimen used to perform electroencephalography in conscious animals has been described. This regimen was reported to limit spontaneous movement in conscious animals, while reducing the effects of deep sedation or general anaesthesia on the recorded EEG. However, this report describes the use of high doses of acepromazine, a drug that may decrease seizure threshold. As discussed above, the association between seizures and acepromazine is still unclear and its use in animals with pathological causes of seizure activity should be performed cautiously.

ANALGESIA FOR PATIENTS WITH NEUROLOGICAL DISEASE

Gabrielle Musk & Anthea Raisis

INTRODUCTION

Pain is defined by the International Association for the Study of Pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or expressed in terms of such damage. Recognition of the presence of pain and assessment of the severity of pain are essential for optimal management and are integral steps towards appropriate treatment of pain in animals with (and without) neurological disease. Poorly managed pain is a significant contributor to morbidity and mortality, has adverse welfare implications and delays the return to normal function. Good pain management relies on regular pain assessment and includes the administration of analgesic drugs (**419**).

The aims of pain treatment are to:

- Inhibit the neuroendocrine stress response, which may compromise recovery.
- Maintain tissue perfusion.
- Allow restful sleep.
- Encourage mobility.
- Improve appetite.
- Attenuate peripheral and central sensitization.

A plethora of drugs exist that can be used alone or in combination to manage pain in animals with neurological disease. Analgesic therapy must be tailored to each individual animal based on the cause, duration and severity of pain, the level of consciousness, the presence of coexisting diseases and the impact of expected side-effects (**420,** p. 559). This chapter describes specific considerations for selecting analgesic agents for pain management of animals with acute neurological disease and provides examples of analgesic regimens that may be suitable for these patients. The physiology of pain and the pharmacology of analgesic drugs are beyond the



▲ 419 (a) A dog following hindlimb amputation with inadequate analgesia. (b) The obvious difference in this animal's behaviour is demonstrated after adequate analgesia was provided.

scope of this book, but a good understanding of both is vital to ensure optimal pain management (see Further reading). Furthermore, familiarity with available drugs will guide the clinician's decision making.

Painful stimuli may cause an acute pain response and poorly managed pain can lead to neurophysiological changes that are permanent. Furthermore, certain types of pain are particularly difficult to manage and require a multimodal approach. The clinician should be prepared to trial therapy and assess the response before committing to a long-term plan. Neuropathic pain is particularly difficult to manage and is often not responsive to opioids. It is produced by peripheral and central sensitization and may be present as allodynia or hypersensitivity (*Table 107*). It may be continuous or sporadic and is described as burning, shooting, tingling or electric in nature.

Table 107 **Neuropathic pain**

TERMINOLOGY	DEFINITION
Allodynia	A pain response to a non-painful stimulus. This is usually localized to the area of the initial injury
Hypersensitivity	An exaggerated pain response to a painful stimulus. This phenomenon occurs as a result of 'sensitization'
Peripheral sensitization	'Wind up' of peripheral nociceptors leading to an exaggerated pain response to stimulation
Central sensitization	'Wind up' of central nociceptors leading to generalized exaggerated pain response to stimulation

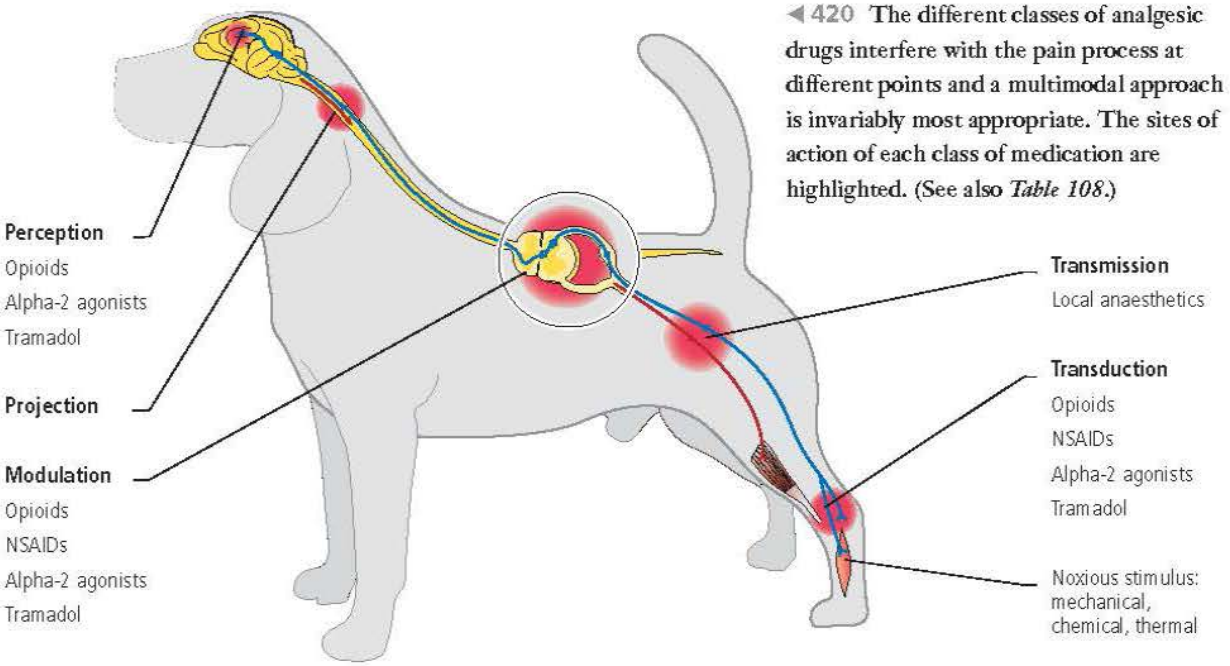
Pain assessment

Accurate assessment of pain in animals is difficult. In animals with acute neurological disease it is even more challenging, especially if a patient is moribund or depressed. Conversely, physical examination may reveal tachycardia, tachypnoea and hypertension, which complicates objective assessment of autonomic nervous system activity. These cases are easy to misinterpret and concern about the adverse effects of analgesic drugs may influence clinical decision making. Given the scope and variability of responses to painful stimuli in human patients, every effort must be made to perform a thorough pain assessment in each animal patient and treat accordingly. Furthermore, assessment of the response to therapy is essential to ensure that pain is adequately and continuously controlled.

In human medicine, self-reporting of pain is the gold standard method of pain assessment. In veterinary medicine, pain assessment has been performed somewhat subjectively or by applying pain scales used in humans. These include simple descriptive scales, numerical rating scales and visual analogue scales. There are inherent limitations with each of these scales; they are one-dimensional and they have been shown to be unreliable in the setting of acute postoperative pain in dogs. They have, however, had their place in the evolution of pain assessment in animals and have contributed to the understanding of the complexity of the pain experience.

Table 108 **The multiple steps of the nociceptive pathway**

TERMINOLOGY	DEFINITION
Noxious stimulus	A mechanical, chemical or thermal stimulus that causes pain. Pain is the sensory and emotional experience associated with actual or potential tissue damage resulting from a noxious stimulus
Transduction	Processing the noxious stimulus from the peripheral site to the sensory nerve endings
Transmission	Signalling along sensory nerves to the central nervous system. Sensory nerves may be small myelinated A fibres associated with sharp mechanical-type stimuli or unmyelinated C fibres associated with dull, burning or longer lasting pain
Modulation	Alteration of the incoming signal by synapsing in the dorsal horn of the spinal cord. Neurotransmitters are involved in the propagation of ongoing impulses in the central nervous system. Synapses within the grey matter of the spinal cord also connect with the ventral horn to complete the reflex arc. This manifests as a withdrawal response to a noxious stimulus



◀ 420 **The different classes of analgesic drugs interfere with the pain process at different points and a multimodal approach is invariably most appropriate. The sites of action of each class of medication are highlighted. (See also *Table 108*.)**

The only validated pain scoring system for acute pain in dogs is the Glasgow Composite Measure Pain Scale (GCMPS), which is a multidimensional scale taking into account not just the intensity of pain, but its consequences. The GCMPS is based on psychometric principles that are well established in human medicine for the measurement of complex constructs such as intelligence, pain and quality of life. It categorizes and weights spontaneous and evoked behaviour and interactive and clinical observations (comfort, vocalization, mobility, demeanour, posture, attention to surgical wound and response to touch), resulting in a composite score. It is practical in a clinical setting and easy to become familiar with and use. As it forces the assessor to evaluate behaviour that may be associated with pain and draw conclusions about whether or not the animal requires additional analgesia, it contributes to improved pain management.

A short form of the GCMPS for dogs suffering acute postoperative pain has been developed for use in a clinical setting where the emphasis is on speed, ease of use and guidance for provision of analgesia as opposed to precise measurement of pain in a research environment. The short form comprises six behavioural categories (vocalization, mobility, demeanour, posture, attention to surgical wound and response to touch). The maximum pain score is 24 (or 20, if mobility is impossible to assess) and it is reported that a clinical decision point for analgesia gave an intervention level of 6/24 (or 5/20 if mobility could not be assessed).

Analgesic drugs

Analgesic drugs fall into the following categories:

- Opioids.
- NSAIDs.
- Local anaesthetics.
- Alpha-2 adrenoceptor agonists (e.g. medetomidine).
- N-methyl-D-aspartate antagonists (e.g. ketamine).
- Miscellaneous drugs (e.g. gabapentin, tramadol, nitrous oxide).

Most analgesic drugs will diminish pain; they are hypoalgesic in effect, rather than entirely abolishing it. The effects are usually dose dependent and an understanding of nociceptive pathways, pain transmission, modulation and perception, the chemical mediators of pain and inflammation and their impact on pain processing will help the decision-making process (**420** and *Table 108*). The different classes of analgesics interfere with the pain process at different points and a multimodal approach is invariably most appropriate.

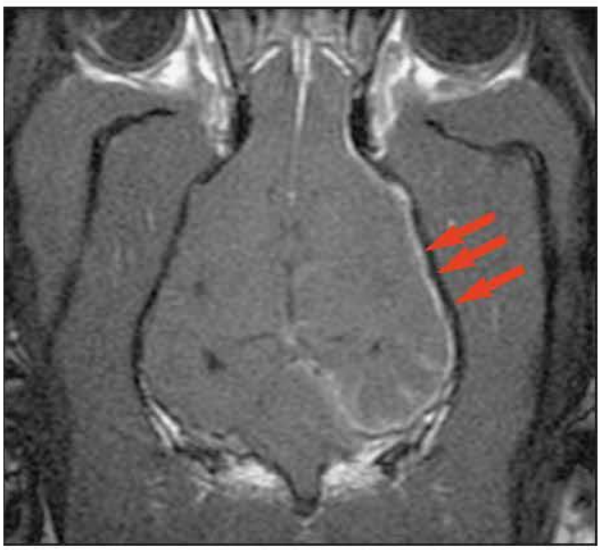
INTRACRANIAL DISEASE

Overview

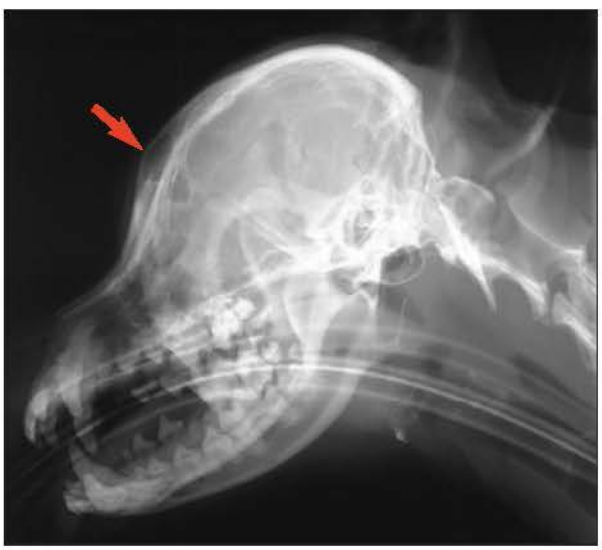
Management of pain in animals with intracranial disease is important from a welfare perspective and because pain itself may increase ICP. This occurs because of sympathetic nervous system-modulated increases in BP.

Considerations

- **Cerebral perfusion**. Selected analgesic drugs and management techniques should have little impact on regulation of CBF. Minimal depression of the cardiovascular and respiratory systems is important for maintaining adequate cerebral perfusion and oxygenation while minimizing secondary neuronal injury. Hypoventilation and consequent hypercapnia may increase CBF and therefore increase ICP, while hyperventilation and hypocapnia may cause cerebral vasoconstriction and compromise CBF. Higher doses of opioids may contribute to hypoventilation through respiratory depression, while pain may cause either hypoventilation if chest excursions are uncomfortable or hyperventilation if the pain is poorly managed. Close monitoring of pulmonary function and careful adjustment of doses are required to provide appropriate analgesia without respiratory depression.
- **Neurological assessment**. Analgesic drugs often cause tranquillization or sedation. Caution should be exercised if these side-effects are likely to impede assessment and mask neurological deterioration. Low doses of short-acting drugs are preferable and a neurological examination should be performed prior to the administration of any medication.
- **Severity of pain**. As nociceptors are present in the meninges and skull, the severity of pain will depend on involvement of these structures in the disease process. Animals with meningitis (**421**) or skull fractures (**422**) are expected to suffer from severe pain and should be treated accordingly. Animals with concurrent trauma to other body systems are also expected to suffer severe pain.



▲ 421 Meningitis is suspected based on the meningeal enhancement present in this dorsal T1-weighted post-contrast MR image (arrows). This condition can be extremely painful. (Photo courtesy Victoria Johnson)



▲ 422 Radiograph of a frontal bone fracture (arrow) in a dog. This lesion would be expected to contribute to the pain present in the animal following its head trauma. (Photo courtesy Victoria Johnson)

Drug selection

Opioids

Opioids are often administered to patients with intracranial disease. A summary of the characteristics and dose regimes of commonly used opioids is presented in *Table 109*.

Full mu agonist opioids can be reversed in the event of undesirable side-effects. The potential complications of opioid administration, particularly important to animals with intracranial disease, include bradycardia (with potential hypotension) and respiratory depression (with associated hypercapnia). Hypotension associated

Table 109 **Opioid analgesic agents used for perioperative pain control in dogs and cats with neurological disease**

AGENT	ADVANTAGES	DISADVANTAGES	DOSE
Morphine	Excellent analgesia (full mu agonist). Can be infused intravenously	Nausea and vomiting may occur, but are more likely if given to a pain-free animal. Histamine release is reported following rapid IV injection	0.1–0.4 mg/kg IV/IM* q2–6h** CRI: 0.05–0.1 mg/kg/hour
Methadone	Excellent analgesia (full mu agonist). Moderate duration of action. Antagonizes NMDA receptors	Pharmacokinetics in small animals unclear. May accumulate with repeated dosing	0.1–0.4 mg/kg IV/IM* q2–6h**
Oxymorphone (US)	Excellent analgesia (full mu agonist)	Bradycardia, respiratory depression, sedation occur at conservative doses	0.05–0.2 mg/kg IV/IM
Hydromorphone (US)	Excellent analgesia (full mu agonist)	Hyperthermia associated with >0.1 mg/kg. Vomiting (especially with SC injection)	0.05–0.2 mg/kg IV/IM
Pethidine (meperidine US)	Good analgesia (full mu agonist)	Potent releaser of histamine when given IV. Pain on IM injection. Large volume. Short duration of action (1–2 hours)	2–5 mg/kg IM/SC q1–2h**
Fentanyl	Excellent analgesia (full mu agonist). Short duration of action (15–20 minutes). Suitable for infusion	High doses cause respiratory depression and bradycardia	CRI: 3–24 µg/kg/hour; transdermal patches: 2–5 µg/kg/hour
Remifentanil	Excellent analgesia (full mu agonist). Short duration of action (3 minutes). Suitable for infusion	Short duration of action (3 minutes). Higher doses cause respiratory depression and bradycardia	CRI: 3–24 µg/kg//hour
Tramadol	Analgesia for moderate pain. Capsules and syrup available for oral administration	May cause nausea, vomiting, dizziness. Increases risk of seizures in susceptible patients. Use cautiously with head injuries	1–2 mg/kg PO/IM/IV q6–12h
Buprenorphine	Long duration of action (6–8 hours). May provide more analgesia than morphine in cats	Analgesia for moderate pain (partial mu agonist). Prolonged onset of action (30–60 minutes)	dog: 0.006–0.01 mg/kg IV/IM/SC* q6–8h; cat: 0.005–0.01 mg/kg IV/IM q4–8h.
Butorphanol	Good sedative	Analgesia for mild pain (kappa agonist). Short duration of action (1–2 hours). mu receptor antagonist	0.05–0.4 mg/kg IV/IM*

* Where a dose range is given, the lower doses are recommended for IV administration (where specified) or IM injection in depressed animals and the higher doses for IM administration in alert animals/animals in pain.

** Cats may have slower metabolism and may require less frequent administration.

CRI = continuous rate infusion.



▲ **423** **Pupillary dilation in a cat after premedication with an opioid.**

with opioid-induced bradycardia is not common in normovolaemic patients with normal myocardial function. Often, the arterial BP remains stable or improves as the increased time during diastole associated with the slight reduction in heart rate allows for improved ventricular filling and an increased stroke volume. Conservative doses of opioids are unlikely to cause significant respiratory depression in normal dogs and cats, but in those with increased ICP the effects may be more marked. Care should be taken and therefore the adequacy of ventilation should be closely monitored. Opioids are also reported to cause pupillary constriction in dogs and pupillary dilation in cats (**423**), which has the potential to interfere with neurological assessment. In conscious animals these side-effects do not appear to be a problem at the low doses used clinically. However, in animals with CNS depression, these side-effects can be exacerbated.

Animals in severe pain, without pre-emptive analgesia (e.g. trauma)

The use of short-acting reversible opioids, such as fentanyl or remifentanil, is preferred in patients in severe pain. These drugs have a relatively fast onset and short duration of action, giving them a pharmacokinetic profile suitable for infusion. The infusion rate can therefore be titrated to achieve the desired clinical effect. A balance between adequate analgesia and minimal CNS, cardiovascular and respiratory depression (and increase in $PaCO_2$) must be achieved. Patients with high ICP may be extremely sensitive to the sedative, cardiovascular and respiratory depressant effects of opioids, so great care should be taken and conservative doses should be administered in the first instance. The authors have observed markedly reduced mentation using low infusion rates of fentanyl. It is recommended that infusions of fentanyl are started as low as 1 µg/kg/hour in animals with head trauma and increased gradually to achieve the desired level of pain management without causing further deterioration in mentation. When analgesia cannot be achieved without respiratory depression, the application of IPPV (manual or mechanical) will be required to maintain normocapnia.

Animals with moderate to severe pain (e.g. postoperative period), having received pre- and intraoperative analgesia

Intermittent dosing of full mu receptor agonists (e.g. methadone, 0.1–0.4 mg/kg IM) may be adequate for animals with severe to moderate pain. However, pain management can only be achieved by maintaining a stable therapeutic plasma concentration of drug. This in turn ensures a stable, effective (e.g. brain or peripheral nociceptor) concentration of drug. To achieve a stable plasma concentration of opioid, an infusion that can be adjusted according to clinical effect is best. Intermittent 'bolus' dosing will cause periods of relative overdose and periods of relative underdose. Morphine and other opioids that may induce emesis should not be used if there is any contraindication to vomiting (e.g. raised ICP). The use of tramadol for perioperative analgesia is currently popular, but there are only a few reports in the literature documenting its use and efficacy in dogs. While it may be appropriate for animals in moderate to severe pain, it is the authors' opinion that it should be reserved for use as an adjunct to an analgesic protocol. A reported side-effect of tramadol in humans is seizures, and while this seems to be a risk for veterinary patients as well, it is unknown how significant a problem this may be. If the patient is receiving other medication that affects the reuptake of serotonin, drug interactions should be taken into account. In such cases a low dose of tramadol or an alternative analgesic drug should be used.

Animals with mild pain

Mild pain can be managed with drugs such as buprenorphine (0.01–0.02 mg/kg IM q4–6h) or pethidine (2–5 mg/kg IM q1–2h). The appropriate interval between drug administrations will depend on the anticipated duration of action of an individual drug. It is always better to aim for a continuum of pain control, so regular dosing is important. To achieve a continuum, subsequent doses of drug should be administered before the plasma concentration of the drug has decreased. Pethidine is a full mu agonist, but it does not produce analgesia comparable to morphine, methadone or other full mu agonists. It is often associated with an increase in heart rate as it has an atropine-like structure. Pethidine should only be given intramuscularly as the potential for histamine release following intravenous injection is high. Furthermore, pain associated with intramuscular injection and the frequent dosing required for continuous analgesia make pethidine a less desirable option for pain management compared with other opioids.

Other agents

A summary of other agents available for use in animals with neurological disease is presented in *Table 110*. NSAIDs are also useful, but if any contraindication is identified (e.g. circulatory shock, coagulopathies, gastric mucosal bleeding, corticosteroid administration, renal disease), they should be avoided. Ketamine should be avoided in patients with intracranial disease and associated increased ICP, as they may be exacerbated by ketamine. Alpha-2 adrenoceptor agonists should be used with extreme caution, as their vasoconstrictive effects may further compromise CBF. Corticosteroid administration may contribute to pain management in certain disease processes (e.g. meningitis or neoplasia associated with marked peritumoural oedema) through their anti-inflammatory action. However, corticosteroids may potentiate neuronal ischaemia in a hypoxic environment (see Chapter 20).

Table 110 **Non-opioids used as part of pain management in animals with spinal disease**

AGENT	ADVANTAGES	DISADVANTAGES	DOSE REGIMEN
Benzodiazepines: diazepam, midazolam	Muscle relaxation	Disinhibition in healthy animals. Respiratory depression in animals with underlying respiratory disease/ insufficiency	Diazepam: 0.1–0.2 mg/kg IV/PO. Midazolam: 0.1–0.4 mg/kg IV/IM
Phenothiazine tranquillizers: acepromazine	Anxiolysis, sedation	Hypotension; avoid in hypovolaemia. Contraindicated in carbamate and organophosphate poisoning	0.01–0.05 mg/kg IV/IM
Alpha-2 agonists: medetomidine, dexmedetomidine	Sedation, muscle relaxation, analgesia. Dexmedetomidine is associated with fewer cardiovascular side-effects than medetomidine	Adverse cardiovascular effects: avoid in animals with heart disease, hypovolaemia. Hyperglycaemia: avoid in diabetics and head trauma. High incidence of vomiting in cats	Medetomidine: bolus, 1–2 µg/kg IV up to 3–5 µg/kg IM; CRI, 0.5–3 µg/kg/hour. Dexmedetomidine: Bolus, 1 µg/kg IV; CRI, 0.5–1 µg/kg/hour
NMDA antagonists: ketamine, amantadine	Analgesia. May be useful to treat neuropathic pain. Interferes with central sensitization. Reverse tolerance associated with prolonged opioid administration	Dysphoria associated with accumulation of norketamine with prolonged infusion, therefore requires dose reduction with time. Arrhythmogenic: avoid in chest trauma. Increased skeletal muscle tone may potentiate pain due to muscle spasm. Pain on IM/SC injection. Cerebellar dysfunction reported anecdotally in some breeds of cat	Ketamine: CRI, 5–10 µg/kg/minute (can be used with morphine or lidocaine CRI). Amantadine: 3–5 mg/kg PO q24h

(Continued)

Table 110 **Non-opioids used as part of pain management in animals with spinal disease** *(continued)*

AGENT	ADVANTAGES	DISADVANTAGES	DOSE REGIMEN
Tricyclic antidepressants: amitriptyline	May be useful in the treatment of neuropathic pain. Blocks noradrenaline and serotonin reuptake in the brain, increasing the effect of these neurotransmitters	Vomiting and diarrhoea, excitability, arrhythmias. Consider drug interactions if using anaesthetics or antiepileptics. Enhanced sedation if used with other sedating drugs	1–2 mg/kg PO q12h
Lidocaine	Analgesia. May be useful in neuropathic pain	Sedation may interfere with mobility. Myocardial depression can cause hypotension in unstable patients. Vomiting reported. DO NOT USE IN CATS	Initial bolus of 2 mg/kg followed by 20–50 µg/kg/minute
Gabapentin	Supplementary analgesia for neuropathic pain	Sedation and ataxia	Titrate dose from 2 mg/kg up to 10–20 mg/kg PO q8–12h

SPINAL DISEASE

Considerations

- **Neuronal function**. Aiming to preserve neuronal function by maintaining perfusion and oxygenation is vital. Agents that cause excessive depression of cardiovascular and pulmonary functions should be avoided. Arterial BP and adequacy of ventilation (using a capnograph) should be monitored closely.
- **Pain**. Pain associated with spinal disease (**424**) is likely to be severe, necessitating the use of potent analgesic drug combinations by continuous infusion.



▲ **424** **Animals with spinal disease, such as the one in this picture, will be in pain and require administration of analgesic agents.**

- **Anxiolysis**. Anxiety in weak or paralysed animals may decrease the pain threshold. The judicious administration of anxiolytics is a useful part of pain management in haemodynamically stable animals.
- **Muscle relaxation**. The administration of muscle relaxants is useful in reducing pain associated with muscle spasm. (*Note:* Do not use in animals with unstable fractures.)
- **Neuropathic pain**. When present, neuropathic pain is often resistant to opioid analgesia and requires a multimodal analgesic regime.
- **Multimodal analgesia**. A combination of analgesic agents can be administered concurrently to optimize pain management and minimize the frequency and severity of side-effects associated with individual agents.

Drug selection

Opioids

Due to the severity of pain in most animals with spinal disease, opioid analgesics are often the best choice. The advantages and disadvantages of commonly used opioids and appropriate dose rates are described in *Table 109*.

Animals in severe pain (e.g. spinal trauma)

As previously described for animals with intracranial disease (see above), the use of short-acting reversible opioids, such as fentanyl or remifentanil, is preferred in animals with severe pain (e.g. trauma victims with multiple organ damage and orthopaedic injury).



▲ **425** Steps for placement of a fentanyl patch. (a) Clip the skin prior to placement of the patch. (b) Wipe the skin with a dry swab only. (c) Wear gloves when positioning the patch. In this case two patches are being used (25 µg/hour and 50 µg/hour). (d) Ensure even adherence to the skin with gentle digital pressure. (e) Cover the patches with a light adhesive dressing and label with the name of the drug and the time and date of application.

Stable animals requiring intensive pain control

During the immediate post-trauma or post-surgical period, the continuous infusion of opioids (e.g. fentanyl or morphine) is more likely to prevent breakthrough pain. Opioid infusions can be combined with other agents to achieve multimodal pain management (e.g. an opioid in combination with ketamine and/or lidocaine). Infusion rates for each of the individual drugs are provided in *Tables 109* and *110*.

The transdermal delivery of drug from a patch applied to the skin (e.g. fentanyl patches, **425**) may provide a useful adjunct to perioperative analgesia. It may take up to 24 hours for therapeutic plasma concentrations to be achieved, so analgesia will be required until this time. The delay is shorter in cats than in dogs. Because there is also marked individual variation in absorption and, therefore, plasma concentrations achieved, fentanyl patches should not be relied on as the

sole method of providing analgesia. Buprenorphine patches are also available and should be used with the same caveats as fentanyl patches. Patches should not be cut in half. If a lower dose is required, then creating a barrier between the patch and the skin is most appropriate. It is best to place the patch on a clipped area of skin out of reach of the patient. The lateral thorax, dorsum or neck may be appropriate.

Stable animals requiring less intensive pain control

When less intensive management of the animal is required, intermittent administration of full mu opioids such as methadone or morphine can be used. Although vomiting is less likely in animals in pain, the use of morphine is generally avoided in animals with cervical injury where violent movements associated with vomiting can cause further injury to an unstable spinal lesion. In addition, recumbent animals that vomit may not be able to clear vomitus from the pharynx and mouth, predisposing to airway obstruction and aspiration.

Other agents

A variety of other agents can be used in conjunction with opioids to improve pain management. A summary of these agents can be found in *Tables 110* and *111*.

Non-steroidal anti-inflammatory drugs

NSAIDs may be used to decrease inflammatory pain and they are potent analgesics in their own right. The cyclo-oxygenase inhibitors carprofen, meloxicam and meclofenamic acid are registered for perioperative use (*Table 111*). The lipoxygenase and cyclo-oxygenase inhibitor tepoxalin was available to the veterinary market, but it has been associated with an increased incidence of adverse side-effects.

Concurrent administration of NSAIDs and corticosteroids is contraindicated due to increased risk of gastrointestinal ulceration and haemorrhage, therefore the use of NSAIDs is best delayed until it has been decided whether the patient will benefit from corticosteroid therapy. For animals receiving either steroids or NSAIDs, concurrent administration of gastrointestinal protectants may help reduce the incidence of gastrointestinal ulceration.

Muscle relaxants

Benzodiazepines (diazepam or midazolam, 0.25–0.5 mg/kg PO q6–8h) may provide a useful adjunct to pain management in patients with stable spinal injury by alleviating muscle spasm, which is commonly observed in animals with spinal disease. In animals with unstable spinal lesions (e.g. fractures), skeletal muscle relaxation may be detrimental as it reduces the splinting effects of the epaxial muscle.

Alpha-2 agonists, such as medetomidine, can also be used to provide muscle relaxation. In addition, these agents are analgesic. Because of sedative and cardiovascular side-effects, these agents are generally limited to animals that do not have cardiovascular pathology. The authors have found that infusing medetomidine at 1–3.5 µg/kg/hour is useful in healthy dogs that have pain or anxiety that is unresponsive to other drugs. As with benzodiazepines, these agents should be avoided in animals with unstable spinal fractures.

Anxiolytics

Acepromazine is an extremely useful agent for anxious animals with spinal disease. Due to its hypotensive effects, the use of this agent should be limited to normovolaemic and normotensive animals. The side-effects are dose dependent; the authors use 0.01–0.05 mg/kg to a maximum of 1 mg/kg. Acepromazine is also more effective if combined with an opioid (e.g. 0.03 mg/kg acepromazine with 0.3 mg/kg morphine for sedation). Trazodone can also be used for this function (see p. 545).

N-methyl-D-aspartate antagonists

Ketamine is becoming increasingly popular as part of a multimodal analgesic protocol in small animals. Ketamine interferes with the process of CNS sensitization (wind-up), which may manifest as hyperalgesia (exaggerated pain response to a painful stimulus) or allodynia (pain response to a non-painful stimulus) from peripheral and central sensitization. It plays an extremely important role in the management of animals with chronic pain, animals with direct nerve trauma, amputees and trauma patients. Care is required when using this agent in trauma patients where the arrhythmogenic effects of ketamine may exacerbate myocardial contusions or

Table 111 **Non-steroidal anti-inflammatory drugs**

DRUG	SIDE-EFFECTS	DOSE RATE: DOGS	DOSE RATE: CATS
Carprofen	Minimal. Vomiting	2 mg/kg PO, SC or IV q12h or 4 mg/kg q24h	2 mg/kg SC once only
Meloxicam	Minimal. Diarrhoea	0.2 mg/kg PO, SC or IV q24h then 0.1 mg/kg q24h thereafter	0.1–0.2 mg/kg PO or SC once only. 0.1 mg/kg q24h for 3 days
Meclofenamic acid	Vomiting and diarrhoea	1–2 mg/kg PO q24h	Not used

ischaemia and associated arrhythmias. At higher doses the cardiovascular effects of ketamine can become problematic (increased heart rate and BP). The authors use 2–10 µg/kg/minute by infusion for analgesia (higher end of dose rate if intraoperatively and lower end if conscious). A 'bolus' dose of ketamine may be incorporated into a premedication for cats (5–10 mg/kg) and very difficult dogs (1–2 mg/kg). Dogs are more prone to the dissociative effects of ketamine, so lower doses should be used in this species. As part of an induction combination, ketamine can be given at 5 mg/kg with a benzodiazepine (e.g. diazepam or midazolam, 0.25–0.5 mg/kg).

Methadone may also act as an antagonist at the NMDA receptor and this is thought to be especially beneficial in the treatment of neuropathic pain that may otherwise be resistant to typical opioids.

Lidocaine

The effectiveness of this agent in spinal pain has not been determined. It should, however, be considered if pain is unresponsive to other agents. It can be administered either alone or in combination with morphine and/or ketamine. Infusion of each drug is adjusted to optimize analgesia but minimize sedation. Lidocaine can depress cardiovascular function and contribute to hypotension, therefore it is essential that animals are normovolaemic and that cardiovascular function is monitored during administration. It should also be used cautiously in cats and at lower doses than in dogs, as the former species is more sensitive to the neuroexcitatory effects of lidocaine.

Lidocaine patches are also available and may be useful for topical analgesia prior to attempting vascular access or for the management of incisional pain. The onset of action is relatively rapid. (The area should be clipped and the patch secured in position to avoid inadvertent ingestion by the patient. Care should also be taken to avoid heating the area, as this may accelerate absorption and increase the potential for side-effects.)

Tramadol

Tramadol is an agent with weak mu opioid agonist and non-opioid analgesic properties. The non-opioid effects are associated with increased noradrenaline (norepinephrine) and 5-hydroxytryptamine (serotonin) at central neuronal synapses, which reduces the excitability of spinal nociceptive activity, partly via alpha-2 adrenergic activity. The activities of the opioid and non-opioid mechanisms are synergistic, resulting in greater analgesia than that expected for each component acting separately. The efficacy of tramadol postoperatively in humans appears to be similar to that of µ opioid agonists. It can be administered parenterally and enterally. Comprehensive clinical studies in animals are currently lacking. Tramadol has a wide therapeutic margin and while most dosing is based on anecdotal reports it is common to use 1 mg/kg q12h or q8h.

NEUROPATHIC PAIN

Neuropathic pain (**426**) is classically less responsive to opioids and difficult to manage. It may occur in patients with lumbosacral disease, neuropathy, nerve root trauma and a number of other conditions. Other agents that may be useful in animals suffering neuropathic pain include ketamine, amantadine, medetomidine, lidocaine, tramadol, gabapentin and tricyclic antidepressants. A summary of these agents and doses rates are found in *Table 110*.

Gabapentin's mode of action in the treatment of neuropathic pain is thought to be by prevention of the release of glutamate in the dorsal horn via interaction with the alpha-2/delta subunit of the voltage-gated calcium channels. While gabapentin has been used safely in dogs, only anecdotal reports of its efficacy have been published.

NEUROMUSCULAR DISEASE

Considerations

- **Severity of pain.** The type of NM disease will influence the severity of pain and the choice of analgesic agents. Some conditions may not be painful, so careful pain assessment is essential.
- **Ventilation.** Animals with NM disease frequently have impaired ventilation. This may be exacerbated by drugs that depress spontaneous ventilation (e.g. opioids).
- **Vomiting.** Animals with NM disease may not be able to protect their airway. In addition, vomiting may trigger laryngeal spasm in animals with tetanus. Agents that predispose to vomiting (e.g. morphine) should be avoided.
- **Sedation.** The use of analgesic agents with sedative properties may exacerbate recumbency and immobility in animals with NM weakness. In contrast, sedation can be useful in animals that are hyperaesthetic (e.g. polyradiculoneuritis). (*Note:* Acepromazine is contraindicated in methiocarb and organophosphate poisoning.)

Drug selection

Any of the drugs used for management of spinal pain can be used for management of animals with painful NM disease. The choice will depend on the stability of the animal and the severity of the pain.

Regional and local anaesthesia in animals with neurological disease

While pain associated with intracranial disease and generalized NM disease is not amenable to regional anaesthesia, this modality may be useful for managing pain associated with trauma to other regions of the body. Regional anaesthesia may also be used in certain spinal diseases. Regional and local anaesthesia provide the ultimate in analgesia if the innervation of an area can be isolated and completely desensitized.

In patients with chest wall trauma, intrapleural or intercostal nerve blocks are effective as an adjunct to an analgesic regime. A maximum dose of 2 mg/kg of bupivacaine should be administered every 6 hours. For intrapleural analgesia this dose may be diluted to increase the volume or combined with $NaHCO_3$ to minimize the discomfort associated with the low pH of the solution. For intercostal nerve blocks, two intercostal spaces either side of the lesion or surgical wound should be blocked (five spaces in total). The intercostal nerves cross-innervate, so it is essential to block at least five spaces. The nerve runs caudal to the rib. Epidural administration of analgesic drugs will provide additional analgesia in animals with concurrent pelvic and abdominal trauma (see Further reading). Epidurals have also been used to provide analgesia in animals with spinal fractures, although the use of local anaesthetic by this route, and consequent motor (and sensory) blockade, should generally be avoided, as motor function is an essential part of neurological assessment. Local anaesthetic drug preparations may be diluted to minimize motor blockade (e.g. 0.25% bupivacaine can be diluted to 0.125%) or ropivacaine may be used. Epidural administration of local anaesthetics should be avoided in haemodynamically unstable animals as sympathetic nerve blockade will

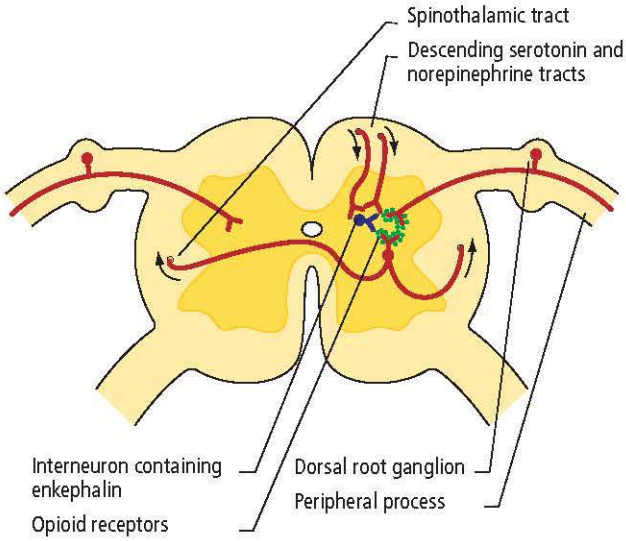
exacerbate hypotension. In these cases, epidural administration of morphine alone (0.1 mg/kg diluted in sterile saline to the desired volume) can still provide useful regional analgesia. The volume of injection is a factor that determines the degree of cranial spread of the drug and, therefore, the clinical effect. Opioids are lipophilic, so will spread cranially, but increasing the volume of injection will facilitate this. As a rule of thumb, 1 ml of diluted drug per 4.5 kg to a maximum of 6 ml is appropriate.

For infiltration of surgical or traumatic wounds, a combination of lidocaine with $NaHCO_3$ (1 mmol/ml) in a ratio of 9:1 will help reduce irritation on injection. Lidocaine 2% can be combined with 0.5% bupivacaine in a 1:1 ratio to provide a more rapid onset and longer duration of action.

Prior to placement of an intravenous or intra-arterial catheter, a eutectic mixture of local anaesthetic (EMLA) cream can be applied to the site at least 30 minutes beforehand. EMLA will facilitate painless placement of a catheter and is especially useful for arterial catheterization in conscious patients. Lidocaine patches are also useful in this situation. For nasal cannula or urinary catheter placement, topical application of a local anaesthetic, such as xylocaine or lidocaine spray, is helpful if administered a few minutes beforehand.

Non-specific aspects of pain management in animals with neurological disease

- Bedding should be well padded, able to wick moisture away from the patient, easy to clean and easy to replace as often as required.
- A comfortable ambient temperature will help prevent hypothermia or panting.
- A urinary catheter may be necessary to prevent urinary retention, especially if an epidural has been administered. Placement of a urinary catheter also facilitates the measurement of urine output, which is useful to ensure adequate fluid therapy and renal function (see Chapters 31 and 2, respectively). Placement of the urinary catheter must be performed aseptically.
- Any wounds should have regular dressing changes. If dressings are wet or odorous, they should be changed immediately.
- Patients that require exercise should be managed carefully by skilled personnel with a good understanding of the individual patient's history and treatments.
- ICUs can be busy places and animals may find it difficult to sleep quietly and rest. It is important to provide quiet times with the lights out, so sleep deprivation does not contribute to morbidity.



◀426 **Neuroanatomy and neurotransmitters involved in pain pathways. Descending pathways modulate the incoming pain sensation, which stimulates glutamate release.**

FLUID THERAPY

Anthea Raisis & Katrin Swindells

INTRODUCTION

Maintenance of normal circulating blood volume and hydration are essential to maintaining adequate perfusion of the brain and spinal cord and form an essential part of the stabilization of animals with neurological disease.

The principles of fluid therapy in animals with neurological disease are generally the same as those in animals with normal neurological function. There are, however, some specific considerations that relate to animals with intracranial disease. These include the following:

- Fluid restriction is associated with increased mortality and is no longer recommended in the management of head trauma patients.
- Adequate oxygen carrying capacity (RBC count) is essential to ensure adequate cerebral oxygenation. An excessive RBC count is also detrimental to cerebral perfusion due to the increased blood viscosity.
- Hypotonic fluids should be avoided when large fluid volumes are required due to the potential for increases in brain tissue water.
- Fluid balance and BP should be carefully monitored. Overzealous fluid therapy associated with high CVP and arterial BP should be avoided, as these will increase the risk of elevating the ICP.
- Normoglycaemia is essential for normal neuronal function, but hyperglycaemia should be avoided. Glucose-containing fluids need to be administered judiciously with close monitoring of blood glucose.
- Normal electrolyte concentrations and acid–base status are important for normal neuronal function.
- Maintenance fluid volume requirements in animals receiving corticosteroids and osmotic diuretics, such as mannitol, are frequently higher than normal.

The first part of this chapter discusses general aspects of fluid therapy, with specific reference to the considerations in animals with neurological disease. Aspects of fluid therapy that are described include types of fluid and rates that can be used in these patients and indications and cautions associated with their use. The second part discusses some specific conditions that alter fluid and electrolyte balance and require special fluid therapy as part of the management of the condition. The final part presents guidelines for use of blood products.

GENERAL GUIDELINES

Types of fluid

Intravenous fluids can be divided into two main types: crystalloids and colloids. The characteristics of these types of fluid and the considerations for use of each fluid in animals with CNS disease are outlined in *Tables 112* and *113* (pp. 572/573).

Administration of fluids

The rate and type of fluid administration will depend on the clinical condition of the animal, red cell count and serum protein levels, electrolyte concentrations and acid–base status. Fluid therapy can be divided into an emergency (resuscitation) phase, a rehydration/replacement phase and a maintenance phase.

Emergency fluid therapy is indicated if an animal is demonstrating clinical signs of circulatory shock caused by an absolute (hypovolaemic shock) or a relative (vasodilatory shock) reduction in circulating blood volume. Shock is defined as inadequate delivery of oxygen to the tissues. Thus, the aim of the emergency phase of fluid therapy is to restore adequate delivery of oxygen and other nutrients to the tissues. Adequate oxygen delivery should be restored within 1–2 hours.

Table 112 **Characteristics of commonly available crystalloid fluids**

TONICITY	TYPE	OSMOLARITY (mosm/l)	COMPOSITION	CONSIDERATIONS
Hypotonic	5% dextrose	252	Glucose ....50 g/l	Administered at up to maintenance rates in hypoglycaemic patients. Avoid hyperglycaemia, which increases secondary neuronal injury. Used to replace free water deficits in patients with hypernatraemia. Hypotonicity increases brain tissue water. Administer at maintenance rates (except neurological disease secondary to acute hypernatraemia). Blood glucose should be closely monitored when administered
	2.5% dextrose/ 0.45% NaCl	280	Glucose ....25 g/l Na .....77 mmol/l Cl.....77 mmol/l	
	0.45% NaCl	154	Na .....77 mmol/l Cl.....77 mmol/l	Hypotonicity increases intracellular brain tissue water. Used to replace free water deficits in patients with hypernatraemia if ongoing losses are minimal. Avoid in intracranial disease (except secondary to hypernatraemia). (See also chapter 27)
Isotonic	Hartmann's solution/lactated Ringer's solution	272	Na .....131 mmol/l Cl.....111 mmol/l K .....5 mmol/l Ca .....28 mmol/l Lactate	Relative hypotonicity may increase brain tissue water when administered in large volumes. Calcium may increase secondary neuronal damage (theoretical). Calcium may combine with citrate in blood products and cause microemboli when coadministered through fluid lines. Lactate will accumulate in liver insufficiency. Avoid in hepatic encephalopathy
	Plasma-Lyte 148 (also consider Normosol R and Plasmalyte-A)	294	Na .....140 mmol/l Cl.....98 mmol/l K .....5 mmol/l Mg .....3 mmol/l Acetate ....27 mmol/l Gluconate 23 mmol/l	Less likely to increase brain tissue water than Hartmann's when given in large volumes. Magnesium may help reduce reperfusion injury (theoretical). Bicarbonate precursors do not require hepatic metabolism. Can be coadministered with blood products due to lack of calcium
	0.9% NaCl	308	Na .....154 mmol/l Cl.....154 mmol/l	Less likely to increase brain tissue water when given in large volumes. Hyperchloraemic metabolic acidosis may develop when large volumes administered
Hypertonic	7.5% NaCl	2564	Na .....1282 mmol/l Cl.....1282 mmol/l	Useful for rapid low-volume resuscitation (2–5 ml/kg over 5–10 minutes). Osmotic effects will help decrease cerebral oedema. Rapid increase in osmolarity and serum sodium may cause central pontine myelinosis in chronic hyponatraemia
	3% NaCl	1026	Na .....513 mmol/l Cl.....513 mmol/l	Useful for treatment of hyponatraemia in SIADH

SIADH = syndrome of inappriate antidiuretic hormone secretion

Table 113 **Characteristics of commonly available colloids**

	TYPE	PERIOD OF VOLUME EXPANSION (relative duration)	RELATIVE INCREASE IN BLOOD VOLUME	CONSIDERATIONS
Gelatins	Gelofusine Haemacel	++	+++	Rapid renal excretion. Anaphylactic reactions recorded. No reported coagulopathy
Dextrans	Dextran 40	++	++	Should not be used. Renal failure reported. Coagulopathy if exceed 20 ml/kg/day
	Dextran 70	+++		Possible coagulopathy if exceed 20 ml/kg/day
Hydroxy-ethylstarch	Voluven Hetastarch 6% (Hextend®) Pentastarch (Pentaspan®)	+++/+	++/+	Larger molecules may help reduce vascular permeability in SIRS (see Chapter 2). Voluven is less substituted on the starch molecule than hetastarch or pentastarch. Hextend® is a balanced electrolyte solution that resembles the composition of the principal ionic constituents of normal plasma. Possible coagulopathy if exceed 20 ml/kg/day
Hb-based oxygen-carrying solutions	Oxyglobin	++++	+++	NO scavenger; role in secondary neuronal injury unknown. Discoloration of mucous membranes, skin, sclera and urine. Potential for excessive volume expansion. Vomiting has been reported in some patients. Interferes with biochemistry tests, especially those that use colourimetric techniques
Natural	Plasma; FFP	+	+	Inefficient colloid (COP = 20). Weak source of albumin. Source of clotting factors, AT (FFP only)

COP = colloid osmotic pressure; PVE = plasma volume expansion; AT = antithrombin; FFP = fresh frozen plasma; NO = nitric oxide.

This does not necessarily require correction of the entire fluid deficit. (For more detail on causes and clinical signs of circulatory shock see Chapter 2.)

The rehydration/replacement phase is indicated once emergency fluid therapy has restored adequate tissue perfusion. This phase is also indicated in any animal that presents with a deficit in total body fluid that is not causing a significant reduction in circulating blood volume or delivery of oxygen to the tissues and thus is not associated with clinical signs of circulatory shock. For example, an animal that is mildly to moderately dehydrated will have a reduction in total body water of 5–10%, but sufficient circulating blood volume to maintain adequate oxygenation of the tissues. Animals that have lost <20% of the circulating blood volume (where blood volume in dogs = 90 ml/kg and in cats = 60 ml/kg) can usually compensate for this loss by reducing urine output and shifting fluid from extravascular space to intravascular space and, as such, do not have decreased tissue oxygenation. However, in both these cases the fluid deficit still needs to be replaced. The replacement phase can be performed more slowly than the emergency phase, allowing the type of fluid and rate to be adjusted regularly according to changing patient requirements.

Maintenance phase is indicated once all fluid deficits have been replaced, but the animal is unable to maintain fluid requirements orally. The three phases of fluid therapy and the types of fluid used are described below.

EMERGENCY FLUID THERAPY (RESUSCITATION PHASE)

Aims of emergency fluid therapy

The aims of emergency fluid therapy are to:

- Rapidly restore adequate circulating blood volume and tissue perfusion (within 1–2 hours).
- Maintain adequate oxygen carrying capacity (i.e. RBCs).
- Maintain COP (COP >15; total solids (TS)>45 g/l [4.05 g/dl]; albumin >20 g/l [2.0 g/dl]).
- Avoid excessive increases in arterial BP and CVP.

Guidelines for fluid administration during resuscitation

Replacement of circulating blood volume can be performed with a variety of fluid types, including isotonic crystalloids +/– hypertonic crystalloids, colloids and blood products, depending on the type of fluid deficit present. The types of fluid used for initial resuscitation, severe dehydration, loss of high-protein fluids and blood loss are described below.

Initial resuscitation regardless of fluid deficit

Immediate volume resuscitation of hypovolaemic animals is usually performed using a polyionic isotonic fluid. Introduction or change to another fluid type can be made if indicated following initial basic blood work including PCV, TS and electrolytes. In animals with head trauma, Plasma-Lyte 148 and 0.9% NaCl offer theoretical advantages over Hartmann's and may be the preferred fluids (see *Table 112*).

The administration of excessively large volumes of isotonic crystalloids for resuscitation can predispose to oedema if an excessive increase in hydrostatic pressure or decreases in COP occurs. In addition, if an animal has suffered significant blood loss (>30% blood volume), the use of crystalloids alone will not compensate for the reduction in oxygen carrying capacity due to the loss of RBCs.

To minimize the detrimental effects of large-volume crystalloid administration, the following protocol is recommended:

- Obtain baseline vital signs (mentation, heart rate, respiratory rate, BP, body temperature), PCV and TS.
- Start with volumes of up to 90 ml/kg in dogs or 60 ml/kg in cats, to be administered in less than 1 hour.
- Monitor mentation and heart rate continuously (ECG is ideal for continuous monitoring of heart rate) and reassess all vital signs every 10–15 minutes (or after 1/4 of the dose has been administered) to assess response to therapy.
- The rate of administration and planned bolus volume is decreased as soon as signs of shock resolve (see end points of resuscitation below). The remaining fluid deficit can then be replaced more gradually. (*Note:* Continue to monitor closely to be sure that the condition of the animal does not deteriorate once fluid rates are decreased. If clinical signs deteriorate and PCV and TS are still within acceptable ranges, resume crystalloid fluid administration at higher rates.)
- Monitor changes in PCV/TS every 30 minutes or after 45 ml/kg and 90 ml/kg in the dog and 30 ml/kg and 60 ml/kg in the cat has been given. If significant decreases in PCV and/or TS occur in animals with ongoing clinical signs of shock, adjustment of the fluid type administered is required (see below).

Resuscitation of animals that fail to respond to initial fluid therapy

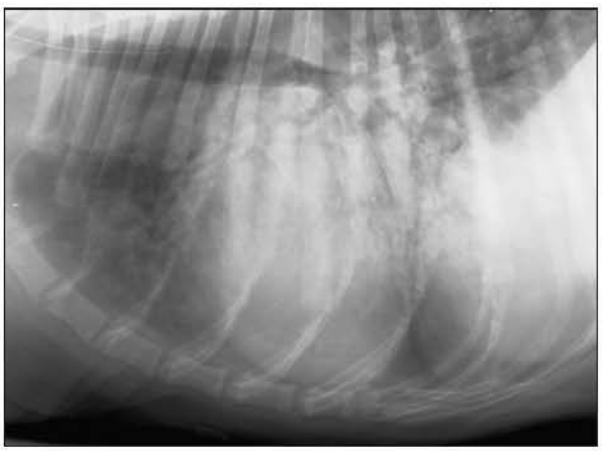
When rapid administration of polyionic isotonic fluids fails to achieve any improvement in tissue perfusion within 30–60 minutes, or the patient is deteriorating, the introduction of other fluids that expand blood volume more effectively may prove useful sooner rather than later. Synthetic colloids can be effective even in animals with normal serum protein concentration. Hypertonic saline also provides rapid expansion of blood volume in animals with haemorrhagic shock. Blood transfusions will help stabilize animals with severe blood loss that fail to respond to initial fluid therapy (**427**). Vasopressors may be required in animals with vasodilatory shock after initial intravenous fluid boluses. (For more details see below and Chapter 2.)

Resuscitation of animals with severe dehydration

Dehydration may occur in any neurological patient that has reduced mobility and subsequently has not had access to water. In addition, animals with CN deficits may appear to be drinking, but may be unable to swallow. Animals with prolonged increases in muscle activity and hyperthermia (uncontrolled seizures; snail bait toxicity) may also develop severe dehydration and associated circulatory shock. Dehydration will cause hypovolaemia once the fluid deficit exceeds >10% of body weight.



◀ 427 If the patient does not improve with crystalloid fluid administration and/or repeat packed cell volume and total solids values (at 30 minutes) are abnormal, addition of another type of fluid is useful. With decreasing packed cell volume and total solids values, blood products should be considered.



◀ 428 In animals prone to pulmonary oedema, as shown in this radiograph of a dog following pulmonary contusions, the use of hypertonic saline or synthetic colloids may be beneficial.

Polyionic crystalloids form the basis of fluid therapy in animals with hypovolaemia caused by severe dehydration (>10–12% body weight). In these animals, polyionic isotonic fluids described above are predominantly used. The first priority is to restore tissue perfusion. Once this has been achieved, the choice of fluid will depend on electrolyte and acid–base abnormalities. Baseline electrolyte levels should be assessed in dehydrated patients when possible. (For management of specific electrolyte abnormalities see below. More details on metabolic derangements can be found in Chapters 3 and 27.)

Resuscitation of animals predisposed to oedema

The use of hypertonic crystalloids and colloids may be useful for resuscitation of animals that are predisposed to cerebral (head trauma) or pulmonary (contusions) oedema (**428**). This will help reduce the volume of crystalloid required to restore blood volume and BP rapidly. In addition, hypertonic saline has the advantage of reducing cerebral oedema due to its osmotic effect.

Hypertonic saline 7.5% is administered at 2–4 ml/kg (cats) or 4–6 ml/kg (dogs) over 5–10 minutes. As with all other fluids, administration is monitored closely and stopped once signs of shock resolve to avoid over administration and excessive increase in circulating blood volume and BP. Serum electrolyte concentrations should be measured to ensure excessive increases in sodium and osmolarity do not occur.

It is important to remember that the effects of hypertonic saline are transitory and that the fluid deficit needs to be corrected with the appropriate fluid type according to the type of fluid deficit present. In addition, administration of hypertonic saline expands the circulating blood volume by drawing fluid from the interstitial and intracellular spaces. This fluid deficit needs to be included in calculations of fluid rates and volumes required for replacement fluid therapy (see below). In animals with chronic dehydration, abnormalities in serum sodium and osmolarity may already exist. In these cases, administration of hypertonic saline is contraindicated.

Resuscitation of animals that have suffered blood loss

Hypertonic saline 7.5% can be administered at 2–4 ml/kg (cats) or 4–6 ml/kg (dogs) over 5–10 minutes in conjunction with polyionic isotonic solutions for initial resuscitation of animals with haemorrhagic shock. This will help expand blood volume more rapidly. If the animal is not responding to crystalloids or the PCV decreases to <0.3 l/l (<30%), whole blood or packed RBCs should be administered (see Principles of blood transfusion therapy, below).

Haemoglobin glutamer-200 (bovine) (Oxyglobin®) has been used to replace blood volume in haemorrhagic shock, although the role of Oxyglobin® in resuscitation of hypovolaemic head trauma patients remains uncertain. Potential benefits include restoration of oxygen-carrying capacity and COP. Potential adverse effects of Oxyglobin® include fluid overload due to the relatively high COP and impaired cerebral perfusion due to the vasoconstrictive effects of nitric oxide (NO) scavenging. Vasoconstriction causes an increase in afterload and associated decrease in cardiac output, which decreases oxygen delivery in some haemorrhagic animal models. The effect of NO scavenging on cerebral perfusion in brain injury is also unknown. The recommended maximum dose of Oxyglobin® is 5–10 ml/kg in dogs and 2.5–5.0 ml/kg in cats.



◀429 **Loss of large amounts of protein can occur in trauma patients with open wounds (as shown in this dog) and large amounts of tissue bruising.**

Resuscitation of animals with hypoproteinaemia

Animals that are, or are expected to become, hypoproteinaemic will require administration of colloids to maintain COP. Protein loss may occur in animals with neurological disease for the following reasons:

- Trauma may have resulted in large exudative wounds or extensive bruising and tissue inflammation (**429**). In these cases, protein will be normal at the time of the accident; however, losses of large amounts of protein-rich fluid can occur during subsequent days following the trauma and if not treated appropriately, these losses can result in circulatory shock and hypoproteinaemia.
- Loss of protein-rich fluid may also occur from the GI tract of any patient that presents with or develops circulatory shock. The GI tract is very susceptible to ischaemic damage, particularly in dogs. Any delay in the correction of circulatory shock can lead to GI tract damage and subsequent loss of large amounts of protein-rich fluid.

Administration of synthetic colloids is indicated when TP is <45 g/l (4.5 g/dl), albumin is <20 g/l (2 g/dl) and/or COP is <15 mmHg. Synthetic colloids are preferred to plasma, as these are more efficient in restoring COP and blood volume. To resuscitate a hypoproteinaemic animal, the rate of polyionic crystalloids is reduced from shock rates to approximately 5–10 ml/kg (higher rates may be required if cardiovascular function does not improve or deteriorates despite introduction of colloid) and colloids are administered at volumes of 10–20 ml/kg/day in dogs and 5–10 ml/kg/day in cats. However, in dogs that are continuing to lose large volumes of protein-rich fluid or if >20 ml/kg/hour is required to stabilize blood volume and prevent death due to hypovolaemic shock, the benefits of administering larger volumes outweigh the risk:

- Fluid overload can occur if excessive volumes are administered. To prevent volume overload, colloids should be administered in increments (1/4 doses) to effect. The rate of administration is reduced as soon as signs of shock improve.

- Coagulopathy has been associated with administration of synthetic colloids. To minimize the risk of coagulopathy the maximum recommended daily amount is 20 ml/kg. Should significant coagulopathy occur, then management includes cessation of artificial colloids and administration of fresh frozen plasma (FFP) and/or fresh whole blood.

End points of resuscitation

During emergency fluid therapy, large volumes of fluids are administered rapidly to restore tissue oxygenation as quickly as possible. Once tissue perfusion has been restored, fluid therapy needs to be reduced to prevent adverse effects associated with continued rapid administration of large volumes. It is not possible to measure tissue perfusion directly in the clinical environment. Indirect assessment of tissue oxygenation can be performed using a variety of clinical variables. Certain laboratory measurements can also provide additional information about adequacy of tissue oxygenation.

Clinical assessment

Cardiovascular variables that can provide indirect assessment of tissue oxygenation include heart rate, mucous membrane colour and capillary refill time, peripheral body temperature, pulse quality, BP and mentation.

Certain target values for these clinical variables have been established as guidelines for the end of the resuscitation phase (see Further reading):

- Mentation: alert and responsive.
- Heart rate (bpm): small dogs <140; large dogs <120; cats 160–200.
- Mucous membrane colour: pink.
- Capillary refill time: <2 seconds.
- Urine output (UOP): >1 ml/kg/hour.
- Body temperature increasing.
- Arterial BP (in animals with intracranial disease): SAP >90 mmHg; MAP >70 mmHg.

(*Note:* While adequate BP is required in these animals, high BP [SAP >140 mmHg, MAP >100 mmHg] should also be avoided as this increases the risk of ongoing haemorrhage and predisposes to increased ICP, reduced CPP and herniation. The presence of the Cushing reflex [systemic hypertension and reflex sinus bradycardia in response to increased ICP] in animals with brain injury may complicate assessment of BP. Thus, increased ICP needs to be ruled out as a potential cause of hypertension, particularly if the heart rate is lower than expected. [For more details see Chapter 20.])

Laboratory assessment

There is increasing evidence that clinical assessment alone does not always provide accurate information about tissue oxygen delivery. Significant tissue hypoxaemia has been observed despite the return of clinical variables to normal. Certain laboratory measurements may provide a better indirect measure of the adequacy of fluid therapy in restoring tissue oxygenation. Laboratory measurements that have been found to be useful for assessing response to fluid therapy include serum lactate concentrations, base deficit, mixed venous oxygen saturation and jugular venous oxygenation (see Further reading).

- **Serum lactate concentrations (normal <2.5 mmol/l).** Lactate concentrations increase during shock when the rate of production in the ischaemic tissues exceeds the rate of elimination of lactate by the liver and kidneys. Changes in lactate concentration are considered more useful than the actual lactate concentration measured. Serial lactate measurements can provide information about the resolution of tissue ischaemia in response to fluid therapy. If treatment of shock is adequate, serial measurements will show decreases in serum lactate concentrations. Measurements should be performed prior to fluid resuscitation and then repeated at the end of resuscitation as indicated by resolution of cardiovascular signs of shock. Further increases in lactate or failure to reduce by at least 50% with treatment indicates ongoing significant ischaemia and either insufficient fluid administration and/or the administration of the wrong type of fluid. Lactate measurements do have limitations in assessing oxygen delivery, particularly in the presence of conditions that interfere with lactate metabolism in the tissues or liver (e.g. sepsis, liver insufficiency, lymphoma).

- **Base deficit (normal -3 to +3).** The measured deficit in the amount of base within the circulation can also provide information about adequacy of oxygen delivery to the tissues. With decreasing oxygen delivery, tissues become ischaemic. There is increased production of hydrogen ions (metabolic acidosis) and as these are buffered there is an associated decrease in the amount of base present (base deficit). The greater the base deficit the worse the impairment in tissue oxygenation. Improvement in tissue oxygen delivery during fluid therapy will be associated with a decrease in the base deficit.
- **Mixed venous oxygen tension (normal 53 +/- 10 mmHg).** Mixed venous oxygen tension can be useful for detecting the imbalance between oxygen delivery and oxygen consumption in the tissues that occurs during shock. In response to decreased oxygen delivery, a greater uptake of oxygen occurs in the tissues, resulting in lower venous oxygen tension. An improvement in venous oxygen tension would be indicative of improved perfusion and oxygen delivery.
- **Jugular venous oxygen saturation.** Can be monitored as an assessment of the adequacy of brain oxygen delivery. Values below 50% suggest inadequate perfusion and oxygen delivery (see Further reading).

REPLACEMENT PHASE/REHYDRATION

During this phase the fluid deficit is replaced more slowly, allowing more controlled correction of fluid and electrolyte abnormalities. The replacement phase of fluid therapy is commenced when resuscitation is successful in restoring adequate oxygen delivery to the tissues. It is also indicated in animals that do not present in shock. This includes animals with mild to moderate dehydration (<10% of body weight) (**430**) or blood loss in the absence of clinical signs of hypovolaemic shock. This generally occurs when <20% of circulating blood volume is lost. As the animal compensates for this blood loss by reducing urine output and redistributing fluid from the extravascular to the intravascular compartment, replacement of the fluid deficit is still required.

During this phase, fluid must also replace ongoing losses (e.g. vomiting/diarrhoea/polyuria) and supply maintenance fluid requirements of approximately 50 ml/kg/day. Maintenance requirements are discussed in more detail below. (*Note:* In animals receiving corticosteroids or osmotic diuretics, higher than normal maintenance fluid volume requirements may be warranted. Fluid rates must be adjusted accordingly.)

Guidelines for replacement fluid therapy

The type and rate of fluid administered during this phase will depend on the type and severity of the fluid deficit (e.g. blood, plasma, body water), the duration over which the loss has occurred and associated electrolyte and acid–base abnormalities.

Blood loss

As long as oxygen-carrying capacity and COP are/remain adequate (PCV >0.3 l/l [>30%]; Hb >80 g/l [8 g/dl]; COP >15 mmHg), crystalloids can be used to replace the remaining deficit. The volume of crystalloid required is 3–4 times the estimated remaining deficit in blood volume, as only 1/4–1/3 of crystalloid remains within the vasculature after approximately 1 hour. In animals with intracranial disease, failure to correct anaemia may reduce cerebral oxygen delivery. Therefore whole blood is the preferred fluid to replace deficits in blood volume if the PCV is <0.3 l/l (30%). Details of transfusion therapy are described at the end of this chapter.

(*Note:* Overtransfusion can be detrimental due to resultant increases in viscosity, which will decrease cerebral perfusion. In human patients with intracranial disease, the ideal PCV is 0.3 l/l (30%), as this provides adequate oxygen-carrying capacity and also produces beneficial rheological properties that enhance cerebral perfusion.)

Loss of protein-rich fluid

Once the signs of shock have resolved, the type of fluid used for ongoing replacement is determined by the COP and TS values. Artificial colloids +/- plasma are used to maintain COP (>15 mmHg). In the absence of COP measurements, colloid administration is recommended if TS are <45 g/l (4.5 g/dl) or albumin <20 g/l (2.0 g/dl). (*Note:* Once administration of synthetic colloids has been performed, interference with refractometer readings will prevent accurate measurement of TS. Therefore, assessment of continued need for colloids is based on clinical signs [presence of oedema] or measurement of COP, TP or albumin.)



▲430 When animals present with dehydration (<10% in this dog) and normovolaemia, replacement of volume deficit can be performed less rapidly.

Table 114 Clinical characteristics of dehydration

DECREASE IN BODY WEIGHT	CLINICAL SIGNS
<5%	No obvious clinical abnormalities
5–10%	Decreased elasticity of skin, slight prolongation of CRT, dry mucous membranes
10–12%	Marked prolongation of skin tent and CRT, dry mucous membranes, sunken eyes
12–15%	Signs of circulatory shock: increased heart rate, decreased pulse quality, cold extremities, decreased BP

BP = blood pressure; CRT = capillary refill time.

Maximum recommended doses of artificial colloids are 20 ml/kg/day in dogs and 10 ml/kg/day in cats. In patients with severe oncotic deficits, doses of up to 40 ml/kg/day in dogs and 20 ml/kg/day in cats may be required; however, there is an increased potential for side-effects, including coagulopathy, with such high doses.

Body water (dehydration)

Rehydration replaces the estimated deficits in total body water. Estimating the deficit in dehydrated animals depends on the clinical abnormalities present. Guidelines for assessing fluid deficits (% body weight) are outlined in *Table 114*.

It is generally recommended that rehydration is performed over half the time frame in which dehydration occurred to prevent sudden correction of abnormalities in osmolarity and electrolyte concentration. As a general guide, half the calculated deficit should be replaced over the first 6 hours and the remaining deficit over the next 18 hours. For patients who have taken 3 days or longer to develop dehydration, the deficit should be replaced at a slower rate to prevent marked changes in sodium concentration.

MAINTENANCE PHASE

The maintenance phase begins when all fluid deficits have been replaced. Maintenance fluid requirements provide fluid to replace the sensible (measureable losses such as urine output) and insensible (unmeasured losses from respiratory tract, wounds, GI tract).

Guidelines for maintenance fluid therapy

Typically, maintenance requirements are approximately 50 ml/kg/day. Maintenance fluid requirements will be higher if either sensible or insensible losses increase. For example, normal urine output is 1–2 ml/kg/day; however, in animals that are receiving corticosteroids or diuretics, increased urine production will necessitate higher fluid requirements. Ideally, the rate of fluid administration should be based on measured urine output. Insensible loss cannot be measured clinically; however, in normal resting animals it is approximately 20 ml/kg/day. Increases in insensible losses of up to 50 ml/kg/day are associated with increased metabolism (fever, hyperthermia) or increased respiratory losses (panting). Insensible losses can be higher due to gastrointestinal loss or secondary to inflammation of the peritoneum or tissues.

For most animals, a polyionic, isotonic fluid, such as Hartmann's solution or Plasma-Lyte 148, is suitable for short-term maintenance. If an extended period of fluid administration is required, these fluids may cause gradual increases in Na^+ and Cl^- concentration. If this occurs, 0.45% NaCl or 0.45% NaCl/2.5% glucose can be administered. Close electrolyte monitoring is required if 0.45% NaCl or 0.45% NaCl/2.5% glucose is administered at greater than maintenance fluid rates. In hypoproteinaemic, normovolaemic animals, synthetic colloids (Voluven, Pentastarch, Hetastarch) can be administered at 20 ml/kg/day in dogs and 10 ml/kg/day in cats to help maintain COP.

Potassium supplementation

Inappetent animals will require potassium (K^+) supplementation during replacement and maintenance phases of fluid therapy (*Table 115*). The use of diuretics, particularly of loop diuretics, will increase renal losses of K^+. The amount of supplementation will depend on the serum K^+ concentration of the animal and the rate of fluid administration, but should not exceed 0.5 mmol/kg/hour. Serum potassium concentrations should be maintained in normal ranges. Maintenance supplementation of KCl for animals that are not eating or are receiving inadequate nutrition is 20 mmol/l in isotonic crystalloid delivered at maintenance fluid rates.

Table 115 Guidelines for supplementation of potassium

Serum potassium (mmol/l)	Supplementation (mmol KCl/l of crystalloid)	Maximum infusion rate (ml/kg/hour)
<2.0	80	6
2.1–2.5	60	8
2.6–3.0	40	12
3.1–3.5	30	16
3.6–5.0	20	25

(Adapted from Greene RW, Scott RC (1975) Lower urinary tract disease. In: *Textbook of Veterinary Internal Medicine*. (ed. SJ Ettinger) WB Saunders, Philadelphia, p. 1572.)

Magnesium supplementation

Animals receiving diuretics and inappetent or critically ill animals may develop hypomagnesaemia, which necessitates supplementation. In addition, magnesium is reported to help reduce secondary neuronal injury. However, data on supplementation rates specific for neurological disease are lacking. It is reasonable to extrapolate current critical care guidelines to maintain magnesium in normal ranges. If hypomagnesaemia is present or a total body magnesium deficit is suspected, the recommended rate of magnesium supplementation is 0.15–0.5 mmol/kg/day (0.3–1 mEq/kg/day), with daily monitoring of magnesium levels.

Assessment of fluid therapy during replacement and maintenance phases

Assessment of the adequacy of fluid therapy should include a thorough clinical examination 2–3 times daily. Calculation of fluid balance and measurement of body weight should be performed at least once a day. In addition, measurement of heart rate, respiratory rate, arterial BP +/- CVP and body temperature should be recorded frequently to determine changes that may reflect improvements or deteriorations in blood volume and hydration status. Trends in UOP and urine SG should also be recorded on a regular basis. Guidelines for interpreting the response to fluid therapy using these measurements are provided in *Table 116*. The frequency with which all these measurements should be recorded will depend on the condition of the animal and ongoing losses. In animals where hydration status and fluid losses may be unpredictable, measurements should be recorded every 2 hours, particularly if they were previously suffering from circulatory shock. Once the animal becomes more stable, measurements can be recorded every 4–6 hours.

Fluid balance calculation

Calculation of the fluid balance should be done at least once daily in animals receiving fluid therapy. Fluid balance is the difference between the estimated fluids received and fluid losses.

Fluids received include all fluids administered including water contained in the food fed to the animal (intravenous and oral, water content of food). Fluid losses include all losses including UOP, GI tract losses (vomiting/diarrhoea), insensible losses (see above) and losses of

Table 116 **Guidelines for assessing response to fluid therapy during replacement and maintenance phases**

CLINICAL SIGNS	FLUID BALANCE	BODY WEIGHT	URINE OUTPUT	USG*	CVP	CHANGES TO FLUID PLAN
Dehydrated	Ins < outs (ongoing losses)	< Normal	Low	High	Low	↑
	Ins > outs (losses ceased, but not yet replaced)	< Normal, but increasing	Low	High	Low	↑
	Ins > outs (3rd space fluid losses occurring)	> Normal (3rd space losses)				
Overhydrated	Ins > outs	↑	Low (anuric or oliguric renal failure)	Low	High	↓
			Normal/high (if excessive fluid therapy)			
Normal hydration	Ins = outs	Normal	Normal	Normal	Normal	Maintenance + ongoing losses

USG = urine specific gravity; CVP = central venous pressure.

* assuming normal renal function, no diuretics and the patient is not currently receiving artificial colloids such as Voluven

fluid from the circulation into spaces such as body cavities (pleural/peritoneal effusion). The amount of fluid lost as oedema or into a body cavity (third space fluid losses) can be estimated from inappropriate increases in body weight (i.e. increases in body weight in excess of that expected with replacement of fluid deficit). It is important to remember that inappropriate increases in body weight may also be caused by fluid retention in anuric/oliguric renal failure. This represents an excess of fluid and indicates that a reduction in administered fluid rate and volume is necessary. Insensible losses are respiratory and normal GI tract losses. These cannot be measured, but should be included in calculations of fluid balance. For most animals resting quietly, insensible losses are approximately 20 ml/kg/day. In animals that are panting excessively or have increased body temperature, insensible losses can be up to 50 ml/kg/day.

If the calculated fluid received is less than ongoing fluid loss an increase in fluid administration may be required. Clinical and laboratory evidence of inadequate hydration should also be present to confirm the need for increased fluids.

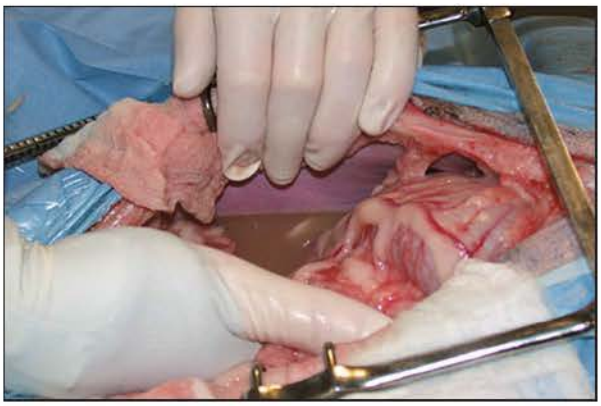
If fluid received is more than fluid loss, one possible cause is an ongoing fluid deficit that has not been adequately replaced. Evidence of the body's attempts to conserve fluid (low UOP and high USG) and a low CVP would support this finding. Continued fluid administration at the planned rates or increased fluid rates if the difference is still large would be required. The exception would be animals with anuric or oliguric renal failure, where failure to produce urine is responsible for the imbalance between fluid in and fluid out. Clinical evidence of fluid retention (e.g. oedema) may help confirm this. In these cases, USG will be low and measurements of CVP will be high.

Serial body weight measurement

Repeated measurement of body weight is a useful guide to assessing fluid therapy during the replacement and maintenance phases. In uncomplicated cases, once to twice daily measurement is recommended. For animals at risk of volume overload (reduced renal function, low COP), more frequent monitoring (4–6 hourly) will provide early detection of fluid retention.



▲ 431 Inappropriate increases in body weight may reflect retention of fluid within the body. This cat has septic peritonitis secondary to traumatic damage to the abdomen and intestine.



▲ 432 Accumulation of fluid within the peritoneum, as seen in this laparotomy, is associated with increased body weight.



◄ 433 Frequent monitoring of urine output and specific gravity is also useful for determining fluid balance. Use of an indwelling catheter and a closed collection system is recommended in critical patients.

Weight loss during the replacement/maintenance phases may represent dehydration due to inadequate fluid administration. Humans with traumatic brain injury have been shown to have significant negative nitrogen balance and weight losses of up to 15% body weight per week (see Further reading), therefore weight loss due to inadequate nutrition should be taken into account when interpreting decreases in body weight. Weight loss due to inadequate nutrition may also mask expected weight gain associated with replacement of fluid deficit.

Weight gain during this phase may reflect replacement of a fluid deficit. If the fluid deficit has been accurately estimated and the fluid therapy is adequate, then weight gain should be consistent with replacement of the estimated fluid deficit. If weight gain is in excess of estimated water deficit, it is possible that the initial estimate was inaccurate. Alternatively, fluid retention/volume overload may be responsible (**431, 432**). If the initial deficit was underestimated, there should be no clinical signs of overhydration. In contrast, clinical signs of oedema (e.g. pitting oedema on limbs, increased respiratory rate, nasal discharge, pulmonary crackles) and a high CVP are suggestive of fluid retention.

Serial packed cell volume/total solids, electrolyte and acid–base measurement

Measurement of PCV, TS, electrolyte and acid–base balance are useful for assessing the effectiveness of volume replacement and also for assessing the appropriateness of the chosen fluid type and rate. During the replacement phase, monitoring should be performed at least twice a day. For animals with severe electrolyte abnormalities, more regular monitoring is recommended (see below).

Urine output and specific gravity measurement

Serial measurement of UOP and USG is also useful for assessing correction of fluid deficits (**433**). UOP below normal (where normal = 1–2 ml/kg/hour) in association with a high USG is supportive of dehydration and reduced renal perfusion. Generally, improvements in UOP together with a decrease in USG from highly concentrated (>1.040) towards minimally concentrated (<1.025) are indicators of improved renal perfusion and correction of fluid deficits during administration of crystalloid fluids.

There are several situations when changes in UOP and USG may not be as expected. Firstly, if large volumes of synthetic colloids have been administered, USG may actually increase, as the excretion of the colloid molecules will alter the refraction of the urine. Secondly, drugs that alter urine production and renal concentrating ability, such as diuretics or corticosteroids, can cause increased UOP and decreased USG despite ongoing dehydration. Therefore, when an animal with neurological disease has recently received these drugs, UOP and urine USG alone should not be used for assessment of fluid therapy. (For more details of monitoring urine output see Chapter 2.)

Central venous pressure measurement

Measurement of CVP is particularly important for assessing fluid therapy in animals at risk of increased ICP. (For more details on CVP monitoring see Chapter 2.)

SPECIFIC FLUID AND ELECTROLYTE DISTURBANCES IN NEUROLOGICAL DISEASE

Metabolic abnormalities that accompany CNS injury are most commonly associated with disorders of water and sodium regulation.

Syndrome of inappropriate antidiuretic hormone secretion

SIADH is caused by antidiuretic hormone (ADH)-secreting neoplasias, excessive ADH release secondary to CNS or pulmonary pathology, drugs, stress and pain. It is characterized by hyponatraemia, hypo-osmolarity, normovolaemia to hypervolaemia and urine sodium concentration >20 mmol/l (> 20 mEq/l). Treatment will depend on the clinical presentation.

In animals that present without clinical neurological abnormalities, free water restriction can be used to gradually increase serum sodium concentration. It is also essential that the underlying cause is corrected.

In animals with neurological abnormalities associated with hyponatraemia, more aggressive therapy is needed. As these animals are either normovolaemic or hypervolaemic, administration of fluids at or in excess of the maintenance rate is not required. 0.9% saline was previously considered a suitable fluid for correction of the sodium deficit in SIADH. However, due to the excessive renal water reabsorption in response to ADH, and sodium losses in response to hypervolaemia and natriuresis, administration of replacement fluids such as 0.9% saline may result in worsening hyponatraemia and is no longer recommended. Administration of 3% saline as a slow continuous infusion in conjunction with water restriction is the recommended therapy for SIADH associated with clinically significant hyponatraemia.

Administration of 3% saline should be calculated to increase serum sodium by a maximum of 0.5 mmol/l/hour or 10–12 mmol/l/24 hours until a serum concentration of 125–130 mmol/l is reached, at which time further correction of serum sodium can be performed by water restriction alone. Serum sodium should be initially monitored every 1–2 hours to assess response and prevent overcorrection.

The volume and rate of administration of 3% saline are calculated as follows:

- The total body sodium deficit is 0.6 × lean body weight × (125 – serum sodium).
- The calculated sodium deficit is divided by 513 (the sodium content [in mmol/l] of 3% hypertonic saline solution) to obtain the number of litres of 3% saline required.
- The required sodium increase (i.e. sodium deficit) in mmol/l is then multiplied by 2 to give the period of time over which the sodium should be infused to ensure that replacement of the deficit occurs at 0.5 mmol/l/hour.
- The volume is then divided by the time period to calculate the rate of fluid administration.
- Electrolytes should be monitored every 1–2 hours initially to assess response.

For example, if a 10 kg dog presents with a serum sodium concentration of 108 mmol/l:

- The calculated total body sodium deficit is 0.6 × 10 × (125 – 108) = 102 mmol sodium.
- The deficit of 102 is divided by 513 to produce a volume of 0.199 l or 199 ml.
- The time period over which this volume is infused is (125 – 108) × 2 = 34 hours.
- Therefore, the infusion rate of 3% saline is 199/34 = 5.8 ml/hour for 34 hours.
- Monitor electrolytes every 1–2 hours. If correction occurs too rapidly, the infusion rate is decreased; if too slowly, the fluid rate is increased.

In some patients, furosemide may be required to increase water excretion. Antagonists of ADH receptors in the kidney (e.g. demeclocycline) are used in humans; however, there is potential for renal toxicity and no specific recommendations for dosages in dogs and cats.

Central diabetes insipidus

CDI is caused by pituitary and hypothalamic lesions secondary to head trauma and intracranial surgery. It is characterized by polyuria, dehydration, hypernatraemia, low urinary sodium and low USG. Other causes of hypernatraemia (see below) associated with treatment of neurological disease need to be ruled out before a diagnosis of CDI is made.

Treatment includes exogenous replacement of ADH with desmopressin or aqueous vasopressin and gradual replacement of the free water deficit with 5% dextrose (intravenously or orally with water).

All the formulae for calculating the free water deficit provide an approximate starting point for fluid rates of 5% dextrose (or oral water). However, the actual rate of sodium decrease will depend on the patient's underlying pathology and ongoing water losses; therefore, sodium levels should be monitored initially every 2–4 hours and fluid rates adjusted to maintain a decrease in sodium of approximately 0.5 mmol/l/hour.

The free water deficit can be calculated as:

- Body weight (kg) × 0.6 × ([measured sodium – normal sodium]/normal sodium – 1). For this calculation a normal serum sodium concentration of 145 mmol/l (145 mEq/l) in dogs and 155 mmol/l (155 mEq/l) in cats is used.
- This calculated volume of water (administered as 5% dextrose) should be infused gradually with the aim of decreasing the sodium concentration by a maximum of 12 mmol/l/day or 0.5 mmol/l/hour.

For example, a dog with a serum sodium of 170 mmol/l (170 mEq/l) (i.e. 25 above normal) should have its free water deficit infused over 50 hours (25 mmol/l ÷ 0.5 mmol/l/hour = 50 hours). Alternatively, 1.9 ml/kg/hour of 5% dextrose will drop sodium by approximately 0.5 mmol/kg/hour.

For patients showing severe neurological signs secondary to hypernatraemia, sufficient free water should be infused over 2–3 hours to decrease the serum sodium concentration by 5–7 mmol/l (5–7 mEq/l), allowing rapid improvement in the severity of clinical signs. Once signs improve, the rate should be immediately reduced to stay within the maximum recommended daily decrease in serum sodium of 12 mmol/l/day (12 mEq/l/day).

Abnormalities associated with treatment of neurological disease

A variety of medications used in neurological disease can lead to fluid and electrolyte abnormalities. Administration of corticosteroids interferes with the concentrating ability of the kidneys and may result in nephrogenic diabetes insipidus. Diuretics can also predispose to excessive water losses. This is of little consequence in animals able to drink adequately. However, animals that have water withheld or stop drinking for another reason are at risk of developing dehydration accompanied by hypernatraemia.

Diuretics can also result in increased urinary loss of a variety of electrolytes from the body with long-term administration including sodium (mannitol), potassium (loop diuretics), magnesium (mannitol and furosemide) and phosphate (carbonic anhydrase inhibitors).

Electrolytes, PCV and TS should be monitored at least once daily in patients who are reliant on intravenous fluid therapy to maintain hydration.

PRINCIPLES OF BLOOD TRANSFUSION THERAPY

Administration of blood products is required in animals that have suffered significant loss of blood or red cells in order to maintain oxygen-carrying capacity and thus oxygen delivery to vital organs such as the brain. In animals with brain injury this is particularly important for preventing secondary neuronal damage due to ischaemia. Administration of blood products is also required in animals that have disorders of primary or secondary haemostasis. Indications for different blood products in neurological patients include:

- Haemorrhage (**434**) (secondary to trauma or surgical losses): whole blood, packed RBCs.
- Anaemia (**435**) (Heinz body anaemia in cats secondary to propofol administration): whole blood or RBCs.
- Decreased number or function of platelets (**436**) (secondary to large volume [>50% circulating blood volume] transfusion of stored whole blood or packed RBCs): fresh whole blood, platelet-rich plasma, or platelet conentrate.
- Decreased clotting factors (cerebral haemorrhage secondary to coagulopathy [e.g. rodenticide]; DIC secondary to prolonged circulatory shock, hypoxaemia): fresh whole blood; fresh frozen plasma.

The following section describes methods for collecting blood for transfusion and provides information on how to determine rates and volumes of blood required to be administered.

Acquisition of blood products

Selection of donors

All donors should be healthy, fully vaccinated, free of blood-borne diseases/parasites and have never previously received a transfusion. Each animal should receive an annual physical examination, CBC, biochemistry and urinalysis. PCV and TS should be checked prior to every transfusion.



▲ 434 Blood transfusions may be required when haemorrhage occurs during surgery. Significant blood loss can occur during spinal surgery, so the suction bottles, such as seen in this figure, should be regularly checked.



▲ 435 Anaemia may occur due to destruction of red blood cells, causing pale mucous membranes as seen in this cat. Treatment may include administration of packed red blood cells.



▶ 436 Animals with reduced platelet numbers or function, associated with clinical signs such as the ecchymoses seen in this dog, can be treated with fresh whole blood.

Canine donors

Docile large breed dogs over 25 kg can donate 450 ml up to once every 3 weeks. Greyhounds are considered ideal.

The main dog erythrocyte antigens (DEAs) include DEA types 1.1, 1.2, 3, 4, 5, 6, 7 and 8. Dogs frequently have more than one type of antigen on their red cells and so can be positive for several blood types. Testing is not available for all blood types. DEA 1.1 is the most antigenic blood type and is associated with acute haemolytic reactions in previously sensitized individuals. Because of the significant potential for stimulating immunoreactivity in naïve dogs, the life span of DEA 1.1 red cells transfused into DEA 1.1 negative dogs can be significantly shorter than expected due to delayed haemolysis. Donors should be DEA 1.1 negative, unless the recipient is DEA 1.1 positive, in which case it can receive DEA 1.1-positive or DEA 1.1-negative blood. Other blood types require prior exposure for reactions to occur. DEA 4 is present in approximately 98% of canines, therefore donors who are positive for DEA 4 and negative for DEA 1.1 are considered ideal donors.

Feline donors

Feline donors ideally should be over 5 kg in body weight. Healthy felines can donate 10 ml/kg of blood.

Feline blood donors should be blood typed. Feline blood types have historically been divided into A, B or AB, with the incidence of different types varying between countries. Within Australia, the majority of cats are type A; the incidence of type B varies geographically up to 39% and type AB is <1%. Within Europe and America, type A is also most common, with type B being variable (reports of 1–6% in the USA) and type AB rare.

Collection of blood

Canines

Ideally, dogs who donate regularly should be trained to lie in lateral recumbency on a table (**437**). However, for less cooperative donors, light sedation with butorphanol (0.2–0.4 mg/kg IV or IM) is often adequate. If not, small doses of acepromazine (0.01–0.02 mg/kg SC) can be used but increase the risk of hypotension in the donor and should be avoided. If the donor requires acepromazine sedation, a peripheral intravenous catheter should be placed in case rapid fluid replacement is required.



▲ **437** **Blood is collected with the dog positioned in lateral recumbency. The weight of the bag is monitored during collection to determine the volume collected.**

Alternate jugular veins should be used in animals donating regularly. Local anaesthesia with administration of subcutaneous lidocaine can increase donor compliance. The collection site is surgically scrubbed. Collection into commercial blood collection bags containing anticoagulant is preferred. To minimize bacterial contamination, care must be taken not to allow air to enter the line or bag. During collection, the bag should be rocked continuously to prevent coagulation occurring. The amount of blood in the bag can be measured during collection by weighing the bag. The collection is finished when the bag has gained 450 g in weight; overfilling bags will dilute the anticoagulant and increase the risk of clots forming.

Felines

Collection of blood from feline donors usually necessitates sedation. Possible sedative regimes include:

- Midazolam (0.2 mg/kg IM) + butorphanol (0.2–0.4 mg/kg IM).
- Midazolam (0.1mg/kg IV) + butorphanol (0.2 mg/kg IV).
- Acepromazine (0.01–0.02 mg/kg IM) + butorphanol (0.2–0.4 mg/kg IM).
- 1–2 mg/kg ketamine + 0.1–0.2 mg/kg diazepam IV.

- Mask induction with sevoflurane or desflurane and subsequent maintenance with an inhalation agent delivered using a mask is extremely useful in very uncooperative donors.

The cat is gently restrained in sternal recumbency with its neck extended or in lateral recumbency. The jugular is clipped and surgically prepared. Collection of blood into syringes containing appropriate amounts of anticoagulant is the easiest way of drawing blood from donor cats. The amount of citrate phosphate dextrose adenine-1 (CPDA-1) or acid citrate dextrose-A (ACD-A) required is 1 ml per 7 ml of blood. Blood is collected via a butterfly needle into either one 60 ml syringe or three 20 ml syringes. Syringes should be rocked to ensure adequate mixing with anticoagulant. Short extension sets on butterfly needles provide sufficient distance from the needle for the syringes to be rocked. Blood collected via syringes should be used within 48 hours of collection, as there is increased risk of bacterial contamination.

Administration of blood products

Ideally, blood products should be at room temperature. All blood products, including packed red cells and plasma, should be administered through a blood filter (in general 170 µm filters should be used). Small volume paediatric filters are best in cats.

The preferred route for administration of blood is intravenously (cephalic or jugular vein), although the intraosseous route can be used in neonates. Selection of catheter size will depend on the rate at which the blood needs to be administered. A shorter catheter with a larger diameter should be selected for rapid administration. Catheter size will also depend on the size of the animal and the vein used. For example, a 20 G catheter is probably the largest catheter that can be placed comfortably in the cephalic vein of an adult cat or small–medium dog, while an 18 G can be placed in a medium–large dog. If a larger catheter is required, placement will need to be into the jugular vein. Absorption from the intraperitoneal cavity is excessively slow, particularly with RBCs.

Blood can be administered in the same line as 0.9% NaCl or Plasma-Lyte 148. It must not be administered with Hartmann's solution (calcium can cause coagulation) or hypotonic solutions such as 5% dextrose, which can cause haemolysis.

Preparation of recipient

Blood typing and cross-matching: dogs

Ideally, cross-matching should be performed in all recipients if time allows. This is particularly important in animals that have had a previous transfusion, as antibodies to transfused blood types will develop within 4–14 days of the transfusion. Cross-matching is essential to avoid blood transfusion reactions if repeat blood transfusions are required more than 4 days after the first transfusion.

Antibodies can also develop in animals that have not been previously transfused. Antibodies to DEA 7 may also occur after exposure to some bacteria. Therefore, dogs should ideally have cross-matching performed even on their first transfusion. However, in dogs that have never previously received a transfusion, the use of non-cross-matched and non-typed canine blood has been used as a life-saving measure. (For details regarding cross-matching, see Further reading.)

Blood typing and cross-matching: cats

Blood typing or cross-matching is essential for all feline recipients (see Further reading for details). Type A cats have weak, naturally occurring antibodies against type B blood. Transfusion of type B blood into a type A cat will result in a delayed transfusion reaction, with markedly shortened RBC survival and potential for an acute haemolytic reaction. Type A cats that received a second type B transfusion would be at high risk for an acute life-threatening haemolytic reaction. Type B cats have strong, naturally occurring antibodies against type A blood and transfusion of type A blood into type B cats causes a rapid and potentially fatal transfusion reaction (after as little as 1 ml of blood). Type AB cats do not have antibodies against either blood type, but should receive either type AB blood or type A blood. There has been recent recognition of a new and probably rare feline blood type Mik, which is present in addition to the A, B and AB antigens. Mik-negative recipients are at risk from acute haemolytic transfusion reaction if they receive Mik-positive blood, even if the blood is correctly typed for the A, B and AB system. Because of the possibility of Mik antigen reactions, all cats should ideally be cross-matched prior to transfusions, even if the donor and recipient blood type are the same.

Premedication

Premedication can be administered, if desired, particularly if cross-matching has not been performed. Suitable premedicants include chlorphenamine (0.5mg/kg IM) and diphenhydramine (2 mg/kg IV).

Rate of administration

Emergency cases

In an emergency (e.g. haemorrhagic shock, DIC with active bleeding) administration of any blood product (whole blood, packed RBCs, FFP) should be commenced at rates of at least 10–20 ml/kg/hour. In cases of massive, acute haemorrhage, blood should be infused as rapidly as possible until clinical signs of shock resolve. As with all resuscitative fluids, continual assessment of response is required to prevent volume overload. As soon as signs of shock resolve, rates of blood administration can be reduced and the remaining deficit in blood volume replaced at a slower rate. (*Note:* Patients who require large volumes of blood products transfused in a short period of time are at risk of developing hypocalcaemia, which may present as muscle fasciculations or hypotension. If this occurs, 10% calcium gluconate is administered intravenously at a starting dose of 0.5 ml/kg.)

Non-emergency cases

In non-emergency situations, infusion of blood products should be started slowly in order to monitor for and minimize the severity of reactions. (For details on blood transfusion reactions see Further reading.)

Typically, the infusion is started at 0.25–2 ml/kg/hour. Vital signs should be recorded (heart rate, respiratory rate, arterial BP, temperature) prior to starting the transfusion and then every 10 minutes for the first 30 minutes. If no reaction has occurred after 30 minutes, the transfusion rate can be increased to up to 4–20 ml/kg/hour. Vital signs should be monitored again 10 minutes after the increase in infusion rate and then every 30 minutes until the end of the transfusion. An example of a form that can be used to monitor animals receiving blood transfusions can be found in the appendices.

In patients with heart disease or at risk of volume overload, the administration rate should not exceed 4 ml/kg/hour. Signs of volume overload include tachypnoea/dyspnoea and a watery nasal discharge. If volume overload occurs, the transfusion should be stopped and diuretics administered and, in cases of severe volume overload where a marked increase in blood viscosity has occurred, phlebotomy should be considered.

In normovolaemic animals (i.e. patients with anaemia or decreased clotting factors), infusion of blood products (i.e. packed RBCs or FFP, respectively) at slow rates is recommended. Concurrent infusion of packed RBCs with a crystalloid solution such as 0.9% NaCl or Plasma-Lyte 148 may be required to reduce the viscosity of the infusion.

Quantities of blood/plasma to administer

Anaemia/haemorrhage

The volume of whole blood or packed RBCs required can be calculated using the following formula:

Actual amount of donor blood needed (ml) = [(desired PCV – actual PCV)/donor PCV] × body weight × circulating blood volume (ml/kg) where:

- Desired PCV = PCV desired at the end of transfusion. After acute haemorrhage a PCV of 0.3 l/l (30%) is generally desirable.
- Actual PCV = PCV of recipient at start of transfusion.
- Donor PCV = PCV of the dog that donated blood.
- Circulating blood volume = 90 ml/kg in dogs and 60 ml/kg in cats.

As an alternative to the above formula, an estimate of the volume of blood required can be made according to the following rule of thumb (calculation based on conventional units and not SI units):

1 ml/kg of packed RBCs or 2 ml/kg of whole blood should raise the PCV by approximately 1%. For example, to increase the PCV from 20% to 30% (i.e. an increase of 10%) in a 20 kg dog, the amount of packed RBCs required = 1 × 20 × 10 = 200 ml, while the amount of whole blood required = 2 × 20 × 10 = 400 ml.

Use of these formulae requires measurement of PCV prior to infusion. In animals that have suffered acute haemorrhage, the PCV changes very little initially and can take several hours to reach the minimum value, depending on the amount of fluid administered. Therefore, the amount of blood/packed RBCs required must be estimated from the severity of clinical signs. With loss of <15–20% of circulating blood volume, sympathetic stimulation and associated responses resulting in increases in heart rate, peripheral vasoconstriction and venoconstriction are usually able to maintain BP and peripheral perfusion. As blood loss exceeds 20%, compensatory mechanisms will be gradually overwhelmed and reduction in BP and tissue perfusion will occur. Hypotension will generally occur when >30% of circulating blood volume has been lost. However, patients who have sustained severe trauma may decompensate at lower volumes of blood loss. Therefore, patients who present with hypotension after acute haemorrhage can be estimated to have lost at least 30% of blood volume and this can provide a starting point for calculating the volume of blood required to be administered. Further volumes of blood are administered until signs of shock resolve.

(*Note:* When large volumes [>50% circulating blood volume] of stored blood are administered, dilution of clotting factors will occur, resulting in coagulopathy. FFP or fresh whole blood should be administered to replace clotting factors [see below].)

Coagulopathy

FFP (**438**) (10–20 ml/kg) should be administered to animals with clotting factor deficiencies that are predisposed to CNS haemorrhage. Patients with DIC may require FFP every 8–12 hours to correct clinical haemorrhage. Fresh whole blood can also be used to correct coagulopathies. However, as greater volumes are required to correct the respective clotting defect, care is required to avoid volume overload (see above).



▲ **438** **After collection, whole blood can be separated into packed red blood cells and plasma. If frozen within 6 hours, the plasma is called fresh frozen plasma. This can be used to treat coagulopathies.**

Cryoprecipitate (one unit per 10 kg body weight) can be used for patients with haemophilia A or von Willebrand's disease. For animals with severe thrombocytopenia, fresh whole blood, platelet concentrate or platelet-rich plasma should be administered to effect to correct the coagulopathy.

Method of administration

As a general rule, blood products should be administered within 4–6 hours of starting the infusion (i.e. 4–6 hours after the drip set was inserted in the bag) and leftover blood products and administration lines should be discarded because of the risk of bacterial contamination. Frozen plasma should be administered within 6 hours of thawing. Gravity administration is generally recommended, as some infusion pumps may cause haemolysis. The fluid pump manufacturer's recommendations must be checked before use.

POSTOPERATIVE SUPPORTIVE CARE AND PHYSICAL REHABILITATION

Sebastien Behr & Rebecca Green

INTRODUCTION

A well-designed rehabilitation plan and a high standard of nursing care will improve the quality of life for an emergency neurological patient and reduce the complications associated with prolonged hospitalization. Failure to provide appropriate supportive care following an acute neurological injury or disease could compromise greatly the chance of recovery due to the development of life-threatening complications (e.g. aspiration pneumonia) or permanent disability.

Rehabilitation is a discipline dedicated to restoring function to an injured or diseased body. Physical rehabilitation covers a wide variety of topics from physiotherapy, hydrotherapy and thermotherapy to ultrasound, acupuncture and electrical stimulation.

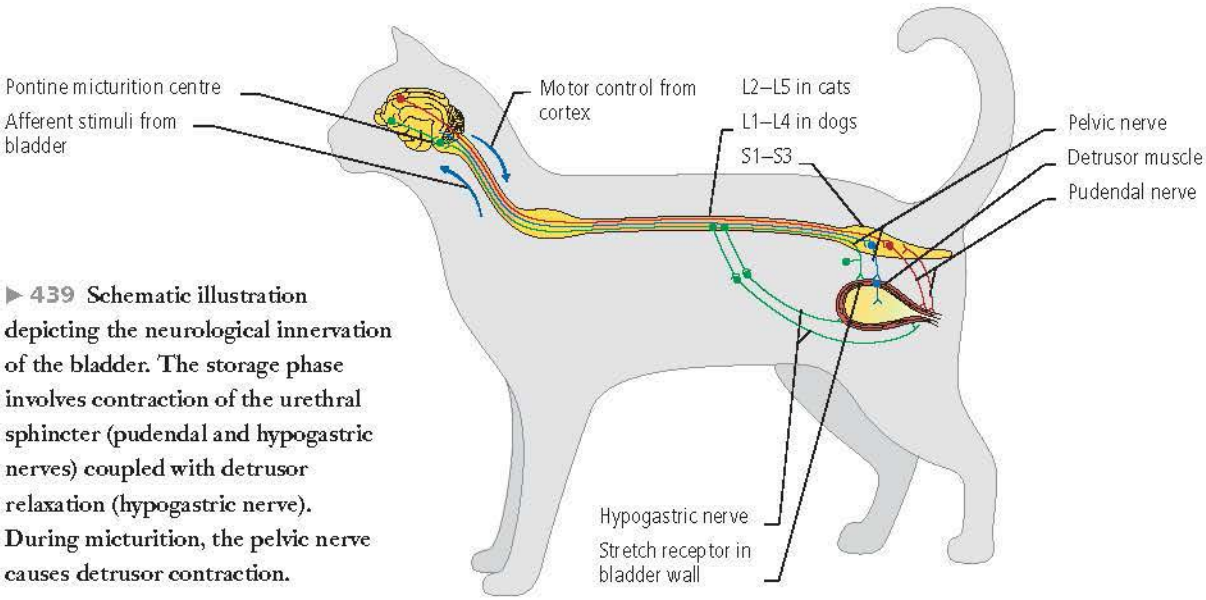
Although clinical signs may improve with time, assuming an appropriate diagnosis was achieved and treatment provided (e.g. decompressive spinal surgery to treat Hansen type I disc herniation), an adequate physical rehabilitation plan may prevent permanent disability and medical complications; in addition, it will accelerate the functional recovery of the patient. Rehabilitation should be initiated as soon as stabilization of the neurological patient is achieved.

This chapter will focus on the supportive care of the neurological patient during hospitalization and on the simple fundamental techniques of rehabilitation that can be performed at the beginning of the recovery period.

SUPPORTIVE CARE

Bladder management

Micturition problems can be seen in patients either with a lesion of the sacral spinal cord segments, their respective nerve roots and peripheral nerves, or with a spinal cord lesion cranial to the sacral spinal cord segments (**439**). The former is described as an LMN disorder and



▶ **439** **Schematic illustration depicting the neurological innervation of the bladder. The storage phase involves contraction of the urethral sphincter (pudendal and hypogastric nerves) coupled with detrusor relaxation (hypogastric nerve). During micturition, the pelvic nerve causes detrusor contraction.**

the later as a UMN disorder. Patients with either a UMN or an LMN bladder may not be able to store and/or eliminate urine effectively and voluntarily. The risks associated with bladder dysfunction include damage to the detrusor muscle caused by overstretching, urinary tract infections, urine scalding and in severe retention syndromes, ureter and kidney damage. The patient's bladder should be checked at regular intervals (every 3–4 hours). Bladder size and urinary status should be documented throughout the day and this should not be based solely on the presence of urine on the bedding.

Pharmacological management

Upper motor neuron bladder disorders

UMN bladder disorders are commonly associated with thoracolumbar spinal cord lesions occurring alongside other neurological deficits (e.g. paraparesis/paraplegia, hindlimb ataxia). These disorders are characterized by a continuous storage phase due to the lack of inhibition of the hypogastric nerve (which causes detrusor relaxation and internal urethral sphincter contraction) and lack of inhibition of the pudendal nerve (which causes external urethral sphincter contraction). Voluntary micturition can be delayed or absent, leading to a distended detrusor muscle while urethral sphincter tone is increased. Manual expression of the bladder is usually difficult.

Treatment

- **Decreasing the internal urethral sphincter tone.** Alpha-adrenergic antagonists such as phenoxybenzamine (0.25–0.5 mg/kg PO q8–12h) or prazosin (dog: 1 mg if less than 15 kg body weight or 2 mg if over 15 kg PO q8–12h; cat: 0.25–0.5 mg PO q12–24h).
- **Decreasing the external urethral sphincter tone.** Skeletal muscle relaxants such as diazepam (dog/cat: 0.2–0.5 mg/kg PO q8h), methocarbamol (20–40 mg/kg PO q8h) or dantrolene (dog/cat: 0.5–2.0 mg/kg PO q12h).
- **Stimulating the detrusor muscle.** Bethanechol for cholinergic stimulation (dog: 2.5–15.0 mg/dog PO q8h; cat: 1.25–5.0 mg/cat PO q8h). Bethanechol should always be given with drugs that decrease the sphincter muscle tone, and bladder size should be monitored closely every 2–4 hours. Usually, the safest option when using bethanechol in patients with UMN bladder dysfunction is to use a concurrent indwelling urinary catheter. It normally takes 3–5 days for bethanechol and phenoxybenzamine to be effective; their individual dosages can be increased at these times if there has not been a satisfactory clinical effect.

Lower motor neuron bladder disorders

LMN bladder disorders are related to diseases of sacral spinal cord segments or the sacral plexus and are usually described as incontinence from urine overflow. Perineal reflex and sensation are usually decreased or absent. The detrusor and the external urethral sphincter are hypotonic. The smooth urethral sphincter tone is intact due to its hypogastric innervation. The bladder is usually easily expressed, but resistance can be found due to the internal sphincter tone (innervated by the hypogastric nerve, which would be unaffected). Pelvic nerve damage is another cause of urinary incontinence and is commonly the consequence of an external trauma. There is a lack of conscious sensation of filling and the bladder is distended. The external and internal sphincters are both constricted. The anal tone and perineal reflex are normal.

Treatment

- **Decrease residual internal sphincter resistance.** Phenoxybenzamine (0.25–0.5 mg/kg PO q12–24h).
- **Stimulate detrusor activity.** Bethanechol for cholinergic stimulation (dog: 2.5–15.0 mg/dog PO q8h; cat: 1.25–5.0 mg/cat PO q8h). It is important, additionally, to empty the bladder regularly (every 2–4 hours) via catheterization or manual expression to limit the risks of retention cystitis and overstretching of the detrusor muscle.

Urinary catheterization

Patients with urinary incontinence should either have their bladder manually expressed or have a urinary catheter placed. Manual expression or drainage of the bladder should be performed every 3–4 hours. Patients that have a urinary catheter placed should wear an Elizabethan collar to prevent interference and have their temperature checked at least twice daily, as unexpected pyrexia may indicate a severe urinary tract infection.



▲ 440 Urinary catheter and collection bag. The bag should always be kept lower than the animal.

Because of patient discomfort, regular catheterization is not ideal even if the risk of infection is not significantly higher than that of indwelling catheterization. Preferably, Foley silicone catheters should be placed and left *in situ* provided no complications occur; they should be maintained in an aseptic manner (**440**). Nevertheless, the risk of urinary tract infection will increase with increased durations of catheterization, therefore the urinary catheter should be removed as soon as voluntary urination is suspected (e.g. recovery of voluntary movement in the hindlimbs).

Urine should be monitored daily for output (1–2 ml/kg/hour), SG and sediment cytology as well as changes in colour and odour. Prophylactic antibiosis for urinary tract infection is not recommended when an indwelling urinary catheter is placed, as it significantly increases the chance of drug-resistant bacterial disease.

Should a long or uncertain recovery of voluntary urination be expected, based on the patient's neurological status (i.e. absence of nociception in the hindlimbs and/or tail and/or perineum), surgical placement of a cystotomy catheter can provide long-term management of urinary retention/incontinence without interfering with the potential recovery of voluntary urination. Several types of cystotomy catheter can be used. These include percutaneous catheters or Foley urinary catheters, which are placed after laparotomy or a minimally invasive inguinal incision.

If possible, patients should still be taken outside. The change of surroundings is beneficial to their mental well-being and may also promote voluntary urination. It is useful to find out from the owners how frequently the patient would normally urinate, any toileting commands and if the patient has a preferred surface to urinate on. Patients should be placed on suitable bedding material (see Bedding) and monitored daily for urine scald.

Management of urine scalding

Urine scalding arises from prolonged contact of urine with the skin (**441**). The onset appears as small erythematous areas, but these can develop into much larger areas. Urine scalding is a lot easier to treat if noticed early in its course. Patients at risk should be monitored daily.

Urine scalding can be relieved by regular cleansing with a mild antiseptic shampoo, clipping the hair around the perineal/inguinal area, applying a barrier cream (e.g. zinc oxide), catheterization if appropriate and using non-retentive bedding.



▲ 441 Severe urine scalding on a paraplegic dog.

Gastrointestinal problems

Diarrhoea and vomiting

GI problems, such as diarrhoea and vomiting, are not unusual during the recovery period of neurological diseases due to possible development of colonic and gastroduodenal ulceration and pancreatitis. Administration of corticosteroids (dexamethasone in particular) and/or NSAIDs will increase the risk of GI problems. Furthermore, diarrhoea and vomiting will increase the risk of complications such as urinary tract infections and aspiration pneumonia, respectively, emphasizing the importance of preventing and treating rapidly such GI disturbances.

Symptomatic treatment is recommended as a first-line approach by discontinuing anti-inflammatory treatment, withholding food for 24 hours, administering intravenous fluids and administration of gastric acid secretion inhibitors such as cimetidine, ranitidine, omeprazole, misoprostol or sucralphate. Unfortunately, none of these drugs reduce the potential of haemorrhage due to GI ulceration subsequent to corticosteroid administration.

Should initial medical management fail or should signs of haemorrhagic gastroenteritis be obvious (e.g. presence of melena), diagnostic tests (haematology and biochemistry including electrolytes, abdominal ultrasound, endoscopy) are recommended to investigate for possible underlying causes (e.g. pancreatitis or GI ulceration).

Bowel management

Similar to micturition, defecation relies on UMN and LMN controlling systems. Most commonly, faecal incontinence arises from neurogenic sphincter incontinence secondary to diseases of the cauda equina (e.g. L7/S1 fracture/luxation, disc disease, neoplasia, vertebral malformation) affecting the LMN system. Damage to the cauda equina results in inability of the anal sphincter to retain faeces and loss of conscious recognition of the passage of faeces. Less frequently, UMN incontinence is present with cranial lumbar, thoracic or cervical spinal cord lesions (e.g. ischaemic myelopathy, arachnoid cysts, neoplasia). These patients are still able to defecate, even with severe spinal injury, due to the reflex action of the GI when stimulated by distension.

It is essential that patients are cleaned as quickly as possible to avoid formation of sores, infection of any wounds, general discomfort and further soiling. Patients that develop diarrhoea should have their perianal and perineal areas clipped, cleaned and protected using a waterproof barrier cream (e.g. zinc oxide). Feeding a low-residue, highly digestible food can assist in the care of these patients by decreasing stool volume and frequency. As with urination, patients should be taken outside to encourage voluntary defecation. It is beneficial to find out from the owners how many times a day the animal would usually pass faeces, any toileting commands and if the animal has a preferred surface to defecate on.

Respiratory problems

Hypoventilation

Patients with brainstem lesions, C1–C6 spinal cord damage and diffuse NM disease can experience hypoventilation leading to hypercapnia. If hypoventilation is suspected clinically, measuring the $PaCO_2$ provides a quantitative evaluation of the efficiency of ventilation (see Chapter 2). Oxygen supply by facial mask, nasal catheter or flow-by delivery should be provided in patients where mild hypoventilation is confirmed, with the method of delivery dependent on the particular circumstances. In severe cases, mechanical ventilation will be required.

Brachycephalic breeds can suffer from severe breathing difficulty with NM conditions or during postoperative/postanaesthetic recoveries due to the conformation of their upper airways. Should severe respiratory compromise be noticed, surgical management (e.g. rhinoplasty and/or palatoplasty) or placement of a tracheostomy tube is recommended.

Patients with respiratory difficulties should have their temperature, mucous membrane colour, capillary refill time, respiratory rate and respiratory effort checked hourly and arterial blood gas checked at least twice daily.



▲ 442 Lateral thoracic radiograph revealing aspiration pneumonia secondary to megaoesophagus.



▲ 443 Feeding a Siamese cat with an oesophagostomy tube.

Aspiration pneumonia

Aspiration pneumonia results from inhalation of stomach/oesophageal contents and is associated with high morbidity and mortality. Aspiration pneumonia can affect the recumbent tetraparetic or tetraplegic spinal patient, but, even more commonly, patients with NM disease, megaoesophagus, regurgitation and dysphagia (**442**).

The most efficient approach to pulmonary aspiration of gastric contents is prevention, which can be achieved by following simple practices:

- **Positioning.** The risk of aspiration pneumonia can be reduced by feeding the patient in a sternal position. Animals with megaoesophagus should be lifted into a sitting position, enabling gravity to assist the movement of food into the stomach. Animals fed in this sitting position should be held for at least 20 minutes after feeding to prevent 'pooling' of food in the oesophagus.
- **Feeding tubes.** For patients that are regurgitating, nothing should be fed by mouth until the regurgitation has stopped. Placing a naso-oesophageal or oesophagostomy tube enables food to enter the oesophagus at a closer entry point to the stomach, reducing the time spent in the oesophagus and consequently the risk of pooling (**443**). The use of naso-oesophageal and oesophagostomy tubes enables the oesophagus to be emptied intermittently by aspiration, helping to reduce the risk of regurgitation. The use of a gastrostomy tube enables food to enter the stomach directly, thus reducing the risk of regurgitation. A gastrostomy tube is the ideal manner in which to feed animals with megaoesophagus; however, placing this type of feeding tube involves GA, unlike the oesophagostomy tube, which can be placed with sedation and analgesia, and the naso-oesophageal tube, which can be placed in conscious/sedated animals.
- **Rest.** In all cases, exercise should be avoided for a minimum of 4 hours post feeding.

Treatment

- **Pharyngeal/oesophageal suctioning.** Should aspiration be witnessed or suspected, suction of fluids and particulates is recommended.
- **Oxygenation.** Humidified oxygen should be delivered by mask, nasal cannula or 'flow-by' tubes to maintain a normal PaO_2.
- **Bronchodilation.** Aspiration will induce bronchoconstriction and administering bronchodilators is recommended (e.g. aminophylline or terbutaline).
- **Nebulization and cupping/coupage.** Nebulization and cupping/coupage (see below) should be performed 3–4 times daily in patients suffering from aspiration pneumonia to humidify respiratory airways and promote coughing, respectively.

- **Fluid therapy.** Intravenous fluids are required to correct hypoperfusion and expand intravascular volume. Care should be taken not to elevate capillary hydrostatic pressure too much, as leakage of fluid into the alveoli will increase pulmonary oedema. However, diuretic therapy is not recommended.
- **Antibiotic therapy.** Antibiotic administration after aspiration without confirmed infection is controversial in human literature, as secondary infection may not necessarily take place and carries the risk of resistant bacterial infection. However, aspiration of oesophageal content carries a high risk of infection and antibiotic therapy is usually recommended for a minimum of 3–4 weeks. A tracheal wash submitted for cytology, culture and sensitivity is indicated before starting antibiotics. Cephalosporins, amoxicillin/clavulanate or trimethoprim-sulphonamide are recommended as first-line treatments of aspiration pneumonia while waiting for culture/sensitivity results. In case of severe infections with suspected resistant gram-negative bacteria, enrofloxacin can be added, but should not be used as a single agent. Patients should be treated for at least 3–4 weeks and 1 week beyond resolution of clinical and radiographic changes.

All animals at risk of aspiration pneumonia should have their body temperature and respiratory rate monitored regularly. Thoracic radiographs are recommended to confirm and monitor aspiration pneumonia 5–7 days after initiating treatment. Radiographic changes may not be seen in the first 24–48 hours after aspiration pneumonia and will usually lag behind clinical improvement.

Pulmonary atelectasis

Atelectasis refers to collapse of part of the lung. It may include a lung subsegment or the entire lung. It is most commonly seen in patients where prolonged recumbency prevents lung expansion. Patients showing signs of atelectasis may be tachypnoeic, dyspnoeic and cyanotic.

To prevent pulmonary atelectasis, patients should be maintained in either complete sternal recumbency or sternal at the front with the hindlimbs moved from side to side every 4–6 hours. Patients that cannot stay in sternal recumbency should be turned between left and right lateral recumbency a minimum of every 2–4 hours.

Cupping/coupage (see below) should be performed 3–4 times daily over both lung fields to promote loosening of secretions developed while recumbent.

Bedding

The most important aspects of the bedding are that it is non-retentive and will allow urine to drain away from the patient. This can be provided by a non-retentive bed (e.g. Vetbed®), a sling bed, a non-retentive bed in its own right, which is raised and allows urine to drain through, or a grate covered by a non-retentive bed that raises the patient off the kennel floor and allows urine to drain from the bed to the floor (**444**).

Recumbent patients require a well padded non-retentive bed to prevent pressure sores (decubitus ulcers, see below). This can be provided by a waterproof foam mattress, a memory foam orthopaedic mattress or multiple thick blankets covered by a non-retentive bed.

Incontinence pads can be placed under the patient's hind end and disposed of once soiled, or under the non-retentive bed to protect against any further soiling of bedding. If the pads are placed under the patient's hind end, it is important that they are removed immediately, as they are retentive and will hold the urine next to the skin, consequently risking urine scalding.

Patients that are not fully recumbent or mobile, but trying to stand, should be provided with non-slip flooring and bedding that is not too soft so as to unbalance them.

Decubitus ulcers

Decubitus ulcers are an ulceration of skin and underlying tissue caused by pressure that limits the blood supply to the affected area. They are caused by the prolonged pressure and friction on the body surface due to the underlying bed.

The most common places for decubitus ulcers to develop are over bony prominences such as the olecranon process of the ulna, cranial aspect of the iliac wing, coxofemoral joint, ischiatic tuberosity and the calcaneal tuberosity.



▲ 444 A grate kennel base providing non-retentive bedding and effective support should the patient be moved.



▲ 445 Decubitus ulcer treated temporarily using circular padding 'doughnuts'.

Prevention of decubitus ulcers is easier than treatment; the following suggestions may help reduce their occurrence. Recumbent patients are at risk of developing these ulcers and therefore require a well padded non-retentive bed; the patient should be turned every 2–4 hours ideally and massage applied to the bony prominences to help promote circulation. Areas at high risk of ulceration can be protected using circular padding or 'doughnuts' of foam (**445**), cotton wool or bubble wrap. The 'doughnut' is placed and secured surrounding the at-risk area, elevating the area from the bedding and thereby promoting circulation. Advanced ulceration will require surgical management. Decubitus ulcers increase the risk of septicaemia and postsurgical infections, and so they should be aggressively treated.

Recumbent patients, where possible, should be lifted into a normal standing position at least twice daily with the use of a hoist or sling; this will not only relieve pressure from the bony prominences and encourage circulation to them, but will also help enhance mental status, strength, endurance and proprioception and help NM awareness (see p. 605).

Hydrotherapy can also be of benefit. The use of a water spa where the patient either stands or is assisted to stand can increase blood flow to affected areas. Water temperature of around 40°C (104°F) tends to increase heart rate.

Intravenous catheter management

Patients may require intravenous fluids or a CRI for a variety of reasons (see Chapter 31). For incontinent patients, intravenous catheter placement would ideally be in either of the cephalic veins, or in the jugular vein if long-term fluid therapy is anticipated. If placement of a catheter in a saphenous vein is necessary in an incontinent patient, it must be checked regularly to observe for signs of infection and redressed as necessary to prevent 'strike-through' to the catheter.

The patient's temperature should be taken at least twice daily to observe for any unexplained pyrexia, which can indicate an intravenous catheter infection.

Jugular catheters should be checked and flushed with heparinized saline every 4 hours and peripheral catheters at least twice daily; however, patients with sensory deficits may need more regular checks, as they may not show the usual signs of discomfort if the catheter is dislodged and fluid is administered perivascularly. Should a catheter infection be suspected, a sample of the catheter tip should be sent for culture and sensitivity, especially in postsurgical patients.

Hypothermia

Hypothermia is a common complication of anaesthesia and surgery, seen mainly in small or toy breed dogs and cats. The initial rapid decrease in core temperature after GA results from an internal redistribution of body heat due to inhibition of vasoconstriction that maintains a large core-to-peripheral temperature gradient. Great care should be taken to maintain and monitor body temperature in patients undergoing GA and surgery. The use of a forced-air warming blanket is recommended during surgery, as it is the most effective method of minimizing anaesthetic-induced hypothermia and rewarming hypothermic patients. An incubator provides the appropriate immediate postoperative environment for recovery in cats or small breed dogs; blankets and heat pads are recommended in large breed dogs. Direct contact of the heat pad on the skin is prohibited due to the risk of developing skin burns.

Exposure keratitis

GA and opioid administration will decrease tear production for at least 24 hours after administration. Regular (every 2–4 hours) and effective eye lubrication is mandatory in patients undergoing GA and/or receiving opioids to prevent development of exposure keratitis. Artificial tears should be applied during anaesthesia, in the first 24 hours following GA and for up to 24 hours after the use of opioids.

Breeds with a relative exophthalmic conformation (e.g. most brachycephalic dogs, Shih Tzu, Lhasa Apso and Cavalier King Charles Spaniel) are prone to lagophthalmos and, thus, increased risk of exposure keratitis. In such breeds, a temporary tarsorrhaphy can be performed as well as regular lubrication with artificial tears.

Pain management

A well designed analgesia regimen is mandatory, particularly for the postsurgical management of patients. The most common drugs used alongside NSAIDs to manage spinal or neurogenic pain include buprenorphine, morphine, methadone, fentanyl, ketamine, medetomidine, dexmedetomidine, lidocaine and gabapentin. The patient's level of pain should be assessed every 2–4 hours using an appropriate pain scoring system. (see Chapter 30 for further details on pain management.)

PHYSICAL REHABILITATION

It is essential that a thorough examination of the patient is undertaken before starting any treatment to avoid deterioration of any pre-existing conditions and to detect any abnormalities that may contraindicate further treatment. The clinical diagnosis should be discussed with the therapist before starting any therapy.

Massage

The benefits of massage are many and it can make a significant difference to recovery. The following section will describe how to perform various massage techniques and their effects. (*Note:* Massage in some patients may cause discomfort. Treatment should be adjusted according to the disease or the time since surgery.)

The effects of and contraindications to massage are listed in *Table 117*. Techniques include stroking, effleurage, petrissage (kneading, compression, picking up, wringing and skin rolling), friction (circular and transverse), percussion (clapping, cupping/coupage, hacking and pounding), shaking and vibration.

Stroking

This is a slow and superficial gliding movement over the body using the entire palm of the hand, usually in the direction of the hair growth, from cranial to caudal and proximal to distal. Stroking is generally considered first as it helps relax the animal, increase blood flow and reduce muscle tone. It can be conducted with the animal in a standing position or in lateral recumbency and can be done both at the beginning and end of a massage session and also between techniques to help loosen tissues.

Effleurage

This is a similar technique to stroking; however, it is carried out in the opposite direction, from distal to proximal, and in a direction towards the heart and lymph nodes (**446**). Effleurage increases venous and lymphatic return by mechanical pressure towards the heart and lymph nodes. It is particularly useful when swelling is present and in between other techniques.

Effleurage decreases muscle tone, stretches muscle fibres, increases the mobility of the superficial fibres and aids in the removal of chemical irritants.

Petrissage

Petrissage techniques are best used on large areas of muscle and consist of five methods: kneading, compression, picking up, wringing and skin rolling.

All five methods have the same effect. They mechanically assist venous and lymphatic return, thereby cleansing the tissues of waste products and assisting circulatory interchange; they increase the length and mobility of fibrous tissue; they restore mobility between tissue surfaces; they aid tissue fluid mobility; and they increase flexibility and strength of connective tissue. If done at a faster rate, they will cause vasodilation and reddening (hyperaemia) of the treated area, and when used slowly they may reduce muscular tension, resulting in relaxation. Sessions of petrissage are best interspersed with plenty of effleurage, to help relax the tissues and disperse any waste products released during the session.

Kneading

This technique comprises rhythmical half circles, with the right hand moving clockwise and the left hand anticlockwise (**447**). The skin in front of the motion is wrinkled and the skin behind the motion is stretched as compression is also applied to the motion. The palmar surface of the fingers or thumbs is used for smaller areas and the palm of the hand for larger areas. Reinforced kneading can be achieved by placing one hand over the other to increase the depth of compression.

Table 117 Massage therapy

Benefits

- Stimulates the lymphatic and circulatory systems, helping to remove metabolic waste products from the muscles and improve blood flow and oxygen supply to the tissues, consequently preparing the tissues for activity and alleviating pain
- Increases tissue circulation, temperature and elasticity, leading to accelerated muscle recovery
- Stimulates the production of endorphins, therefore providing analgesia
- Relieves muscle spasm, cramps and adhesions (scar tissue)
- Improves muscle tone and sensory perception
- Promotes both relaxation and the relationship between the patient and the therapist

Contraindications

- Fever or hyperthermia
- Infection and skin problems
- Neoplasia
- Open wounds
- Unstable fractures
- Acute haematoma
- Heart conditions
- Shock
- Acute inflammation



▲ 446 Effleurage is carried out from distal to proximal, and in direction towards the heart and lymph nodes. It is particularly useful when swelling is present and in between other techniques.



▲ 447 Kneading comprises rhythmical half circles, with the right hand moving clockwise and the left hand anticlockwise. The skin in front of the motion is wrinkled and the skin behind the motion is stretched.



▲ 448 Compression uses the palm of the hand or a clenched fist to apply direct pressure, with no movement of the hand over the muscles.



▲ 449 'Picking up' is mostly used to decongest and relax muscles and is carried out by grasping, lifting and squeezing the muscles.

Compression

This technique uses the palm of the hand or a clenched fist, alternating between each hand rhythmically, applying compression to the muscles and tissues (**448**). This is direct pressure with no movement of the hand over the muscles. Compression should only be applied to larger muscle areas of larger dogs; care should be taken not to overcompress the tissues and hurt the patient.

Picking up

This technique is also known as 'muscle squeezing' and is mostly used to decongest and relax muscles. It is carried out by grasping, lifting and squeezing the muscles between extended fingers and thumb or heel of the hand, maintaining contact at all times (**449**). Picking up is mostly used on the limbs and tail and along the crest of the neck with either one or two hands. It can also be used in a stimulatory manner affecting the nervous system and at a faster rate to help warm up cold muscles.

Wringing

This technique involves using both hands and is mainly used on the patient's back, shoulders and hindquarters. With both hands placed on the patient with the palms against the skin, each hand should be moved in the opposite direction so that one hand brings the tissue towards the operator and the other away (**450**).

Skin rolling

This technique also uses both hands and involves grasping and lifting the skin and superficial tissues between the fingers and thumbs and rolling them either forwards or backwards by drawing the skin towards the thumbs. Skin rolling is useful in detecting adhesions along the back.

Friction

Friction comprises localized small, fast and deep movements given with the tips of the first two or three fingers or the thumb of one hand for smaller areas and both hands for larger areas. It is used to increase blood flow, remove toxins and restore movement between tissues by breaking down adhesions developing over or between tissues as a result of injury or surgery. In combination with kneading, friction can also be used to break down haematoma formation. Friction may cause local hyperaemia by increasing blood circulation and producing a histamine-like substance.

It is essential that these tissues are warmed before applying friction, as well as drained and kept warm using effleurage and petrissage. Friction can be performed in a circular or transverse direction, and when applied causes the superficial tissues to move over the deeper ones. At no time during friction is there any glide of the fingers or thumb on the skin.



▲ 450 Wringing involves using both hands in opposite directions so that one hand brings the tissue towards the operator and the other away.



▲ 451 Hacking is done with the hand at right angles to the muscles, using the ulnar border of the hand with the elbows flexed.

Friction, especially deep friction, can cause discomfort, therefore 2–3 minutes on any one area should not be exceeded. Further inflammation is to be avoided.

Percussion

Percussion, or tapotement, is a soft, rhythmical hitting of the body using alternating hands in a flexible and springy manner. The effects of percussion are an increase in blood circulation, the release of histamine, warming and relaxation of muscles, stimulation of muscle tone and, when used over the lungs, it promotes the loosening of secretions. Percussion consists of clapping, cupping, hacking and pounding.

Clapping

Clapping is done with the elbows flexed, wrists alternating in flexion and extension and the palm of the hand flat against the body. It is performed on muscle groups, not on bony surfaces, apart from the chest.

Cupping/coupage

Cupping/coupage is done with the elbows flexed, the wrists alternating in flexion and extension and the palm of the hand in a cupped/arched position against the body. Cupping can be used all over the body. The cupped area is used to accommodate bony prominences and the hand shape to mould around curved areas, such as the chest.

Hacking

Hacking is done with the hand at right angles to the muscles, using the ulnar border of the hand with the elbows flexed, the wrists extended and the fingers relaxed (**451**). Hacking penetrates deep into the muscles in a gentle manner and is particularly useful for treating back muscles and those of the hindquarters.

Pounding

Pounding is performed using the ulnar side of a relaxed loosely clenched fist with the wrists held in extension. Pounding is only performed after several clapping, cupping and hacking moves to ensure the tissues are warmed beforehand and is usually only performed to provide deep stimulation of the larger muscle groups.

Shaking

This technique stimulates circulation and can also help loosen and move pulmonary secretions. It can be performed using either the fingers or the whole hand, depending on the size of area to be treated. The hand is placed on the skin then the skin is moved with the hand over the muscle structures. This is a highly stimulating technique, so care should be taken around surgical sites and areas of inflammation.

Vibrations

This technique involves no movement of the hand or fingers over the skin surface. The hand is placed on the skin and a trembling or quivering movement applied to the area under the hand. With increasing pressure these vibrations will reach the deeper tissues or joints.

Vibrations can reduce adhesions in well healed scar tissue, soothe swollen joints and arthritic joints and over the lungs can aid in the loosening of pulmonary secretions, making it easier for them to be removed by other massage techniques such as cupping.

Passive range of motion and static stretching

Passive range of motion (PROM) is best described as the full range that a joint or muscle can be moved through with no muscle contraction, using an external force (the therapist) to move the joint (**452**). Joint range of motion (ROM) can be measured using a goniometer; readings are taken of the angle at which the joint is in full flexion and extension. The measurements are re-evaluated at intervals to determine whether there is any improvement or deterioration in the ROM.

ROM can be affected by the structure of the joint and also the tissues that surround the joint; these tissues may be normal or pathological. Paralysed patients, or those with a reduced ambulatory status, are at risk of:

- Joint contracture.
- Reduction in fluidity between the tissues contributing to the formation of adhesions.
- Reduction in blood and lymphatic flow to the limbs, resulting in waste products building up in the muscles, leading to muscle tension and pain.

While performing PROM movements, the joint can be taken beyond the normal ROM and stretched in flexion and extension. Other joints, such as the hip and shoulder, can also be stretched in abduction and adduction. The effects of and contraindications to PROM exercises are listed in *Table 118*.

PROM exercises and stretches will not prevent muscle atrophy or increase strength, as there is no active contraction of the muscle. Even if performed regularly, they will also not eliminate the possibility of muscle contracture, which can only be prevented by the animal regaining functional NM control.

Although the joint should be taken beyond its normal ROM to enable a stretch to occur, it is essential that the tissues are not stretched beyond their limits; this will lead to permanent elongation of the tissues, termed plastic deformation, which may then contribute to joint instability and further immobilization. In older animals the collagen fibres in the muscles become less elastic, and



▲ **452 Passive range of motion of the stifle. The joint is moved in its normal range of motion, in proper alignment, with the proximal and distal bones supported.**

Table 118 Passive range of motion therapy

Benefits

- Improves the flexibility of the tissues and consequently the flexion and extension of the joints
- Prevents contracture of muscles, tendons and ligaments and consequential muscle weakness
- Increases blood and lymphatic circulation, helping to reduce oedema and remove metabolic waste products from tissues and relieve any associated pain
- Prevents the formation of adhesions
- Increases synovial fluid production
- Improves proprioceptive awareness
- Enhances awareness of neuromuscular structure and function

Contraindications

- Fractures (risk of further injury postsurgery or trauma)
- Septic arthritis

so these patients are at a higher risk of overstretching and possible plastic deformation. Care should be taken not to stretch a muscle too quickly, as this will cause the muscle spindle fibre to contract (i.e. muscle shortening and not relaxation), the opposite effect to that desired.

To achieve the most from the session and get the best results from the tissues, it is important that the patient is as relaxed as possible, usually in lateral recumbency on a well-padded mat, or, sometimes, in a standing position. The muscles must have been warmed previously using massage and/or thermotherapy, otherwise there is a risk of tissue damage, especially during stretches. The joint to be manipulated should be moved in its normal ROM, in proper alignment, with the proximal and distal bones supported, to reduce any abnormal stresses on the joint.

PROM exercises should be performed 2–6 times daily, depending on the ROM in the joint. The better the ROM the less frequent the need for the exercises. The movements can be repeated 10–30 times on any one joint. If ROM is normal, or is returning to normal, the frequency can be nearer to 10 times. If the joint has reduced ROM due to contracture or immobilization, the frequency should be nearer 20–30. In a paraplegic patient, PROM movements may be repeated more frequently on the hindlimbs than the forelimbs. All joints, including the digits, on all limbs should be treated, especially if the animal is recumbent, as the normal level of activity will be greatly reduced in all limbs and not just the affected ones.

Stretches should be performed 3–5 times daily and repeated 2–3 times in any necessary position: flexion, extension, abduction or adduction. The stretch is held for 15–30 seconds. Care should be taken not to 'bounce' the joint while it is being held in the stretch, as this can contribute to tissue damage. Stretches of abduction in the hip will help to prevent 'crossing over' of the hindlimbs, seen in paraparetic or paraplegic patients. As ROM improves in the joint, due to an increase in the flexibility of the surrounding tissues, the frequency of the stretches can be reduced.

During all stages of the treatment it is vital that the patient is comfortable. At no time should the patient show any sign of pain by vocalizing or trying to bite. If signs of discomfort are present, the treatment needs to be altered, by reducing the frequency and/or the amount of motion applied to the joint.

It may take several weeks of performing PROM exercises and stretches for any effects to be evident, even when performed many times daily and especially if tissue contracture has occurred.

Flexor reflex exercise

Prevention of muscle atrophy can only be achieved with active muscle contraction, which requires intact NM control. The flexor reflex exercise can provide such active muscle contraction and should be repeated 3–5 times several times daily. Resistance can gradually be applied to the reflex to increase muscle tone and bulk. This exercise is achievable as long as the animal is tolerant and has reduced pain sensation; if it has normal limb pain sensation, this exercise will probably not be tolerated.

Walking/lifting aids

Patients that lack or have reduced motor function of either their fore- or hindlimbs will need aids to help them be moved and lifted. This can be achieved by using:

- An abdominal sling (**453**). Provides support under the abdomen in front of the hindlimbs; can cause the spine to arch. A towel can be used in the same way as the sling.



▶ **453** **Sling support of the hindlimbs of a Dachshund after a hemilaminectomy.**



▲ 454 **Hindlimb harness preventing spinal arching.**

- **A hindlimb harness (454).** Provides support both in front of and behind the hindlimbs and prevents spinal arching.
- **A forelimb harness.** Provides support to the forelimbs.
- **A body harness.** Supports the entire body. Some harnesses are available with lateral supports down the side to help keep the spine straight.

Patients should not be left in a harness when not being moved, as it may rub and cause sores to develop.

Hoists can also be used. They usually have their own integral harness. They are more expensive, but free the therapist to perform further treatment on the patient.

Boots can be used to protect the feet against abrasions and sores while being assisted to move, or, in some cases, self-mutilation while being treated. They should not be left on for long periods as the feet will become hot and sweaty.

Therapeutic exercises

Assisted range of motion

Assisted range of motion (AROM) exercises are performed on patients that have no voluntary motor function, active muscle contraction and/or not enough muscle strength to move the limbs. The therapist has to move the limbs in order to perform the exercise. AROM exercises can be performed in either lateral recumbency or assisted standing. Moving a limb through its normal ROM, as though walking, is an AROM exercise.

These exercises can be performed after the PROM exercises to incorporate the movement of multiple joints in unison. They can be performed 5–10 times on each limb, repeated 3–4 times daily, and have similar effects as PROM. The exercises will assist with:

- Proprioceptive and gait pattern training.
- Neuromuscular re-education.
- Maintaining or improving joint ROM.
- Increasing sensory perception.

As with PROM, AROM will not prevent muscle atrophy as no active muscle contraction is present. The contraindications for AROM are the same as those for PROM (see *Table 118*).

Active assisted range of motion

Active assisted range of motion (AAROM) is indicated when the patient has regained some motor function, muscle contraction is present, but assistance and support are still required. The therapist assists the patient to perform a complete limb movement, where there may be deficits, by assisting the limb to move at the appropriate phase of the gait cycle. This may be while being supported walking on the ground or in water, in lateral recumbency or swimming. As with AROM, it may be advantageous and more productive to perform AAROM exercises after PROM. These exercises will have all of the effects that AROM has, but they will also help to prevent muscle atrophy and increase muscle strengthening due to the presence of muscle contraction and NM control. The contraindications for AAROM are the same as for PROM (see *Table 118*).

Assisted and active assisted standing

Assisted standing is performed when the patient has no ability, or little ability, to hold its own body weight. Active assisted standing is performed when the patient only needs partial assistance and is able to hold the majority of its body weight. This exercise can:

- Encourage weight bearing.
- Assist and enhance NM awareness.
- Promote proprioception and proprioceptive training.
- Prevent decubitus ulcers and atelectasis.
- Encourage urination and defecation.
- Improve mental state.
- Provide the correct posture for eating and drinking, so reducing the risk of aspiration pneumonia.
- Prevent muscle atrophy and encourage muscle strengthening, as well as endurance if weight bearing is evident.

A towel, sling, harness or hoist can be used to perform assisted standing exercises, and for active assisted standing the use of Swiss balls and physio rolls can be added.

Balance and proprioceptive exercises

The aim of these exercises is to improve sensory perception, balance, strength and coordination. The principle is to alter the animal's centre of gravity, which encourages it to shift its weight to maintain its balance. This can be achieved by:

- Weight shifting, which can be done in a cranio-caudal and caudocranial direction using the physio roll or Swiss ball.
- It can also be done from side to side. The animal should have some weight-bearing ability and stand squarely either with or without the support of a sling. The hands are placed on either side of the body and the patient is pushed from side to side. If a sling is being used, this can help to shift the weight from side to side.
- Lifting a limb or gently nudging the animal to the side while walking will alter its centre of gravity and cause weight shifting. Encouraging the animal to follow a treat/ball with its head will also encourage weight shifting. At all times care should be taken not to cause the patient to fall; additional support may be needed while performing these exercises.

Active exercises

Active exercises are considered when the animal is able to move all limbs and bear weight. The exercises will improve muscle strength, endurance and coordination and create more flexion and/or extension of a joint. These exercises do not usually form part of the rehabilitation plan of the emergency patient, but are more part of the plan for the recovering patient.

Hydrotherapy

Hydrotherapy is available in three main forms: hot spa, pool and water treadmill. There are five main principles: buoyancy, hydrostatic pressure, viscosity, resistance and surface tension. The effects and contraindications are listed in *Table 119*. Hydrotherapy is normally not part of the immediate postoperative care. It is usually started 4–6 weeks after spinal surgery. In conditions such as ischaemic myelopathy or NM diseases, hydrotherapy can be initiated straight away assuming no respiratory complications are present.

Table 119 **Hydrotherapy**

Benefits

- Limb movement through decreased load bearing
- Prevents muscle atrophy and assists with standing and therapeutic exercises
- Increases muscle mass, strength, tone and endurance
- Increases sensory perception
- Provides pain relief, relaxation and reduces oedema
- Provides thermotherapy

Contraindications

- Infection and/or skin disease
- Open or draining wound
- Faecal incontinence
- Aquaphobia
- Reduced cardiac function
- Caution with patients having respiratory disease
- Caution with brachycephalic breeds having higher risk of overheating

Thermotherapy/cryotherapy

Thermotherapy

Thermotherapy is the application of heat to the body. There are several ways of applying heat: hot packs, heat pads, hydrotherapy (hot spa) and heat lamps. However, all of these methods have an effect only on the superficial tissues.

Heat should be applied for 15–20 minutes in order to a obtain 3C° (5.4F°) increase in tissue temperature to acquire a therapeutic effect. Once the heat is removed, tissue temperature rapidly decreases because of the vasodilation and increase in circulation. Therefore, exercises/massage should be performed while heat is in place, while the patient is in the hot spa or immediately after the removal of the heat source.

Hot packs should **never** be applied directly to the skin; they should be wrapped in a towel or something similar. Thermotherapy should not be used in the first few days after injury, but can be used 3–5 days post-surgery. The effects of and contraindications to thermotherapy are listed in *Table 120*.

Cryotherapy

Cryotherapy is the application of cold to the body. Cold can be applied using ice packs, cold compression units or ice massage. Cold can penetrate deeper than heat and lasts longer than heat due to the decrease in circulation caused by vasoconstriction.

Ice or ice packs should **never** be applied directly to the skin (except for ice massage); no form of cryotherapy should be applied to a surgical incision.

Cryotherapy should be used in the acute stages of inflammation, in the first 2–3 days after injury, trauma or surgery, or after exercise as a precautionary measure. It should be applied for 15–20 minutes, but the area treated should be checked every 5–10 minutes for signs of frostbite and continually checked after treatment. The effects and contraindications/disadvantages of cryotherapy are listed in *Table 121*.

Table 120 Thermotherapy

Benefits

- Provides pain relief, induces relaxation and reduces oedema
- Softens scar tissue
- Increases flexibility of tissues
- Increases nerve conduction velocity
- Accelerates healing

Contraindications

- Inflammation
- Haemorrhage
- Tumours
- Decreased cardiac function
- Open wounds
- Pyrexia/poor thermoregulation
- Decreased sensory awareness (patients may not be aware of the presence of the heat, therefore they are at risk of developing burns)

Table 121 Cryotherapy

Benefits

- Reduces inflammation and haemorrhage
- Reduces oedema and muscle spasm
- Decreases nerve conduction velocity
- Provides analgesia by stimulating cold receptors and numbing superficial nerve endings

Contraindications

- Areas that have previously had frostbite
- Areas of vascular compromise or patients with poor/reduced thermoregulation
- **Do not** apply ice to a surgical incision or open wound
- Patients that are cold-sensitive. Perform a test area and observe for swelling and wheals on the skin caused by the release of histamine; this indicates cold urticaria
- Care should be taken when applying cryotherapy over superficial nerves to prevent nerve palsy

Therapeutic ultrasound

This treatment should only be performed by a veterinary physiotherapist or other trained personnel. The ultrasound frequencies used are typically between 1 and 3 MHz and penetrate between 0 and 5 cm, affecting both superficial and deeper tissues. Ultrasound can be applied either directly onto clipped skin using a coupling medium, or indirectly by placing the treatment area in water. The effects and contraindications/disadvantages of therapeutic ultrasound are listed in *Table 122*.

Electrical stimulation

Electrical stimulation should be performed only by a veterinary physiotherapist or other trained personnel. The effects of and contraindications to electrical stimulation are listed in *Table 123*.

Types of electrical stimulation include:

- **Neuromuscular electrical stimulation (NMES).** Acts on motor nerves to achieve muscle contraction. Useful for preventing muscle atrophy and increasing/maintaining muscle strength. This method of stimulation is useful for patients that have reduced or no voluntary motor function and are recumbent.
- **Transcutaneous electrical nerve stimulation (TENS).** Does not induce any muscle contraction, but excites the sensory nerves. This provides analgesia to muscles, joints or the spine by activating neural pain control systems. Analgesia is also provided by the reduction in muscle tone, increase in circulation, removal of metabolic waste products and stimulation of endogenous opioids from the spinal cord.
- **Electrical muscle stimulation (EMS)** is used when a muscle is denervated and patients have secondary atrophy (neurogenic muscle atrophy). To achieve muscle contraction in these patients, to prevent atrophy or increase muscle mass and strength, the muscle has to be stimulated. This will need to continue until nerve regeneration has occurred.

Table 122 **Therapeutic ultrasound**

Benefits
• Increases the elasticity of fibrous tissue
• Prevents joint contracture
• Softens scar tissue
• Improves joint mobility
• Reduces muscle tension
• Provides analgesia
Contraindications
• Avoid direct contact with the heart, eyes, gravid uterus, tumours, testes, infected wounds, acute injuries or inflammation, or growth plates
• Avoid areas over the spinal cord following a laminectomy
• Decreased sensory awareness
• Haemorrhage/blood clots
• Open wounds or recent surgical sites to avoid dehiscence
• Decreased cardiac function. Higher risk of burning as the heat is not dissipated as effectively
• Pyrexia/poor thermoregulation

Table 123 **Electrical stimulation**

Benefits
• Increases ROM, muscle strength, tone and function
• Provides analgesia
• Reduces muscle spasm
• Decreases joint contracture
• Corrects gait abnormalities
• Enhances circulation
Contraindications
• Pacemaker placement
• Neoplasia
• Risk of further injury/instability
• Blood clots/haemorrhage
• Inflammation or infection of the area
• Patients at risk of seizure
• Decreased sensory awareness in the area
• Areas of thrombosis or thrombophlebitus

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APPENDICES

Amy Wood, Laurent Garosi & Simon Platt

APPENDIX 1: EMERGENCY DRUG USE

The table below provides selected information on the drug mechanism, dosage and adverse effects of commonly used drugs in neuroemergency patients.

Drugs used in neurological emergencies

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Acepromazine	Phenothiazine tranquillizer Antiemetic	Dog: 0.01–0.02 mg/kg slow IV; 0.01–0.05 mg/kg IM, SC; 1–3 mg/kg PO q8–12h Cat: same dosage as in dog	Can cause significant hypotension. No reversal agent available. Can cause paradoxical excitement, especially in aggressive animals
Acetazolamide	Systemic carbonic anhydrase inhibitor Diuretic	Dog: 5–10 mg/kg IV; 4–8 mg/kg PO q8–12h Cat: do not use	Contraindicated in patients with significant hepatic or renal disease, Addison's disease, hypokalaemia, hyponatraemia or hyperchloraemia
Amantadine	NMDA antagonist (analgesic)	Dog: 3–5 mg/kg PO q24h Cat: Anecdotal use reported at dosages used in dogs	Adverse effects include GI upset, agitation and sedation, especially early in therapy. Use with caution in patients with renal or liver disease, heart failure, narrow-angle glaucoma or seizure disorders. Narrow safety margin; overdosage can cause fatal cardiac arrhythmias, CNS toxicity, hyperthermia, renal dysfunction, and respiratory distress
Amitriptyline	Tricyclic antidepressant	Dog: 1–2 mg/kg PO q12–24h Cat: 0.5–2 mg/kg PO q12–24h	Do not use concurrently with monoamine oxidase inhibitors or anticholinergic drugs. Contraindicated in patients with cardiac arrhythmias, seizure disorders, thyroid disease or adrenal tumours
Atropine	Anticholinergic (muscarinic antagonist)	Dog: 0.02–0.04 mg/kg IV, IM Cat: same dosage as in dog	Contraindicated in patients with tachyarrhythmias, narrow-angle glaucoma or suspected autonomic neuropathy
Azathioprine	Immunosuppressive drug	Dog: 1–2 mg/kg PO q24h, taper to q48h Cat: not recommended	Can cause bone marrow suppression (especially in cats) and hepatotoxicity; hepatotoxicity is idiosyncratic in dogs

(Continued)

Drugs used in neurological emergencies *(continued)*

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Bethanechol	Cholinergic (muscarinic agonist)	Dog: 5–25 mg/dog PO q8h Cat: 1.25–5 mg/cat PO q8h	Do not use in patients with urethral obstruction or increased urethral outflow resistance. Do not use concurrently with other cholinergic drugs or drugs that increase urethral sphincter tone. Adverse effects include salivation, lacrimation, urination and defecation
Buprenorphine	Opioid analgesic; partial agonist	Dog: 0.005–0.03 mg/kg IV, IM, SC, bucally/sublingually q6h Cat: 0.005–0.03 mg/kg IV, IM, SC, bucally/sublingually q6h	Will prevent efficacy of pure mu agonists for 6–8 hours
Butorphanol	Opioid analgesic, mixed agonist/ antagonist	Dog: 0.1–0.6 mg/kg IV, IM, SC, PO q2–4h Cat: 0.1–0.8 mg/kg IV, IM, SC, PO q2–4h	Do not use in patients with pneumonia or other lower respiratory tract disease with copious mucus production (suppresses cough)
Carprofen	Nonsteroidal anti-inflammatory	Dog: 2–4 mg/kg SC, slow IV single dose; 2 mg/kg PO q12h Cat: 2 mg/kg SC, slow IV single dose Licensed at 4 mg/kg single dose in cats	Can cause GI ulceration; do not use in combination with other ulcerogenic drugs (steroids, other NSAIDs, aspirin, methotrexate). Adverse effects include hepatic and renal insults; do not use in dehydrated, hypovolaemic or hypotensive patients or those with GI disease or blood clotting abnormalities
Charcoal, activated	Adsorbent	Dog: 1–4 g/kg PO (granule); 6–12 g/kg PO (suspension) Cat: same dosage as in dog	Adverse effects include emesis (especially when administered rapidly) and constipation. Separate from other oral medications by at least 3 hours. Administer cautiously in sedated patients or those with reduced gag reflex
Clindamycin	Antibiotic Antiprotozoal	Dog: 5–33 mg/kg PO, SC, IM, IV q 8–12h; for Neospora,10 mg/kg q12h concurrently with trimethoprim/sulphonamide Cat: 5–15 mg/kg PO, SC, IV q8–12h; for systemic toxoplasmosis, 12.5–25 mg/kg PO, SC q12h	Use with caution in patients with severe liver or kidney disease and in neonates. GI upset is most common adverse effect. Can cause hypersalivation following liquid administration in cats. Recommend following pills with water to avoid oesophageal injury
Clomipramine	Tricyclic antidepressant	Dog: 1–3 mg/kg PO q12h Cat: 0.25–1 mg/kg PO q12h	Do not use concurrently with monoamine oxidase inhibitors or anticholinergic drugs. Contraindicated in patients with cardiac arrhythmias, seizure disorders, thyroid disease or adrenal tumours
Clonazepam	Benzodiazepine Anticonvulsant	Dog: 0.5 mg/kg PO q8–12h Cat: 0.1–0.2 mg/kg PO q8–12h	Contraindicated with severe liver disease. May lose efficacy after ~3 months. Taper rather than discontinue abruptly after long-term use

(Continued)

Drugs used in neurological emergencies *(continued)*

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Clorazepate	Anticonvulsant	Dog: 0.5–2 mg/kg q8h for 24–96 hours (for management of cluster seizures at home) Cat: use for seizures not reported	Primary adverse effect is sedation, which can be profound. Recommend starting with lower dose and repeating as necessary for cluster seizures between doses. Rapidly induces hepatic metabolism, so not useful as maintenance drug. Contraindicated in patients with severe liver disease or narrow-angle glaucoma. May precipitate fear/aggression
Cyclosporine	Immunosuppressive drug	Dog: 5–10 mg/kg PO q12–24h Cat: 5 mg/kg PO q24h	Vomiting, anorexia, diarrhoea, gingival hyperplasia and papillomatosis. Avoid reaching high blood levels in patients with renal or hepatic disease. Atopica or Neoral (brand names) recommended for reliable drug delivery
Cytarabine (cytosine arabinoside)	Immunosuppressive drug	Dog: 50 mg/m^2 SC q12h, for 4 doses or 200 mg/m^2 IV infusion over 24 hours then every 3 weeks Cat: 100 mg/m^2 SC q12h, then every 3 weeks	Myelosuppression (especially leukopenia) has been reported, with nadir 5–7 days after treatment; recommend monitoring CBC. Can also cause GI upset. Use appropriate precautions when handling. Excreted in urine for 24 hours after administration
Dantrolene	Skeletal muscle relaxant	Dog: 1–5 mg/kg PO q12h; 2–5 mg/kg IV single dose (prevention of malignant hyperthermia); 3–10 mg/kg q8h (urine retention disorder); 0.5–2.0 mg/kg PO q8h with diazepam Cat: 0.5–2 mg/kg PO q12h	Can cause hepatotoxicity. Avoid use in patients with liver disease. Adverse effects include weakness, sedation, GI upset and increased frequency of urination
Dexamethasone	Corticosteroid Anti-inflammatory agent	Dog: 0.1–0.2 mg/kg IV, IM, PO Cat: same dosage as in dog	Causes iatrogenic hyperadrenocorticism (especially in dogs); effects include PU/PD, polyphagia, weight gain, poor hair coat, panting, elevated liver enzymes and insulin resistance, among others. Can cause GI upset, including ulceration, especially if given concurrently with other steroids or NSAIDs (contraindicated). Taper slowly after long-term use. Immunosuppressive doses contraindicated in patients with known or suspected infections
Dextrose solution 5%	Fluid replacement	Dog: 40–50 ml/kg IV q24h (glycaemic control) Cat: same dosage as in dog	Overdosage can lead to hyperglycaemia, dehydration and hyperosmolar syndrome
Dextrose solution 50%	Fluid replacement Antibiotic	Dog: 0.5 g/kg IV bolus, diluted 1:1 with sterile water (hypoglycaemia) Cat: same dosage as in dog	Must be diluted and given slowly to avoid phlebitis. Overdosage can lead to hyperglycaemia, dehydration and hyperosmolar syndrome

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Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Diazepam	Anticonvulsant Benzodiazepine Tranquillizer Skeletal muscle relaxant	Dog: 0.5–2.0 mg/kg IV to effect (emergency management of seizures); 0.5–2.0 mg/kg/hour IV in 0.9% NaCl as CRI (emergency management of seizures); 0.25 mg/kg PO q8–12h (skeletal muscle relaxant); 0.2–0.5 mg/kg IV, IM (sedation or premedication); 1–2 mg/kg rectal (emergency management of seizures) Cat: 0.3–2 mg/kg slow IV slow (emergency management of seizures); 0.5 mg/kg/hour IV in 0.9% NaCl as CRI (emergency management of seizures); 0.25 mg/kg PO q8–12h (skeletal muscle relaxant); 0.2–0.5 mg/kg IV, IM (sedation or premedication); 0.5–1.0 mg/kg rectal (emergency management of seizures); 0.2 mg/kg IV (appetite stimulant)	Contraindicated in patients with severe liver disease. Can cause idiosyncratic hepatotoxicity when given orally to cats. May cause thrombophlebitis, especially if given as a CRI through a peripheral vein. Can cause paradoxical excitement in both dogs and cats
Doxycycline	Antibiotic	Dog: 3–11 mg/kg PO, IV q12h Cat: 3–11 mg/kg PO, IV q12h	Adverse effects include GI upset (recommend giving with food). Can cause oesophageal stricture in cats (follow with water or give in a slurry). Avoid use in pregnant or young animals due to the potential for teeth and bone abnormalities. Antacids affect absorption. Phenobarbital can reduce half-life. Rapid IV administration can cause significant cardiac arrhythmias
Felbamate	Antiepileptic	Dog: 15 mg/kg PO q8h Cat: no data available	Adverse effects may include blood dyscrasias, dry eye, anxiety, inappetence and behaviour changes. Avoid in patients with pre-existing hepatic disease
Fentanyl	Opioid analgesic Pure agonist	Dog: 1–5 mcg/kg IV q15–20 minutes; 2–15 mcg/kg/hour CRI preceded by loading dose; patch: 3–5 mcg/kg/hour Cat: 1–5 mcg/kg IV q15–20 minutes; 2–10 mcg/kg/hour CRI preceded by loading dose; patch: 25 mcg/hour. Kittens <3 kg: half a 25 mcg/hour patch exposed (**do not cut or apply heat**)	Adverse effects include sedation, dysphoria, urine retention and constipation. Causes dose-related CNS, respiratory and cardiovascular depression (bradycardia) that can be profound. Patches may not provide consistent blood levels in veterinary patients; skin irritation at the patch site has been reported. Do not use in patients that have received a selective serotonin reuptake inhibitor or monoamine oxidase inhibitor in the last 14 days

(Continued)

Drugs used in neurological emergencies *(continued)*

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Furosemide	Diuretic	Dog: 2–6 mg/kg IV, IM, SC, PO q8–12h Cat: 1–4 mg/kg IV, IM, SC, PO q8–24h	Do not use in dehydrated patients, patients with electrolyte imbalances or patients in anuric renal failure. Can cause hyponatraemia, hypokalaemia and dehydration. High doses can cause ototoxicity, especially in cats
Gabapentin	Anticonvulsant Analgesic	Dog: 15–25 mg/kg PO q8–12h (antiepileptic);10–15 mg/kg PO q8–12h (neuropathic pain, paraesthesia) Cat: same dosage as in dog	Sedation and ataxia are most common adverse effects. Withdrawal seizures may occur if discontinued abruptly after chronic usage. Separate by at least 2 hours from administration of oral antacids. Use with caution in patients with impaired renal function. Liquid formulation must be compounded, as commercially available liquid contains xylitol
Heparin	Anticoagulant	Dogs:100–200 IU/kg IV, then 100–300 IU/kg SC q6–8h (arterial thromboembolism, DIC);100 IU/kg SC q6–8h (thrombosis prevention) Cat: same dosage as in dog	Do not use in patients with severe thrombocytopenia, hypocoagulability (due to causes other than DIC) or those that may undergo surgery. Overdosage can cause spontaneous bleeding; reversal agent is protamine sulphate
Hetastarch	Colloid	Dog: 1–10 ml/kg IV bolus, then 1 ml/kg/h IV; maximum 50 ml/kg/24 hours IV as CRI Cat: 1–5 ml/kg IV bolus, then 1 ml/kg/hour IV; maximum 50 ml/kg/24 hours IV as CRI, always administered to effect	Do not use in patients in heart failure or oliguric/anuric renal failure due to the risk of volume overload. Use with caution in patients with thrombocytopenia (interferes with platelet function). Can cause vomiting if given too rapidly
Hydrocortisone	Anti-inflammatory	Dog: 0.5 mg/kg PO q12h (anti-inflammatory); 2–4 mg/kg IV, IM q4–6h (acute addisonian crisis) and 0.125 mg/kg PO q12h for maintenance; 1–10 mg/kg IV single bolus (shock)	See dexamethasone
Hydroxyurea	Anti-neoplastic agent	Dog: 50 mg/kg PO q24h 3 days/week Cat: 25 mg/kg PO q24h 3 days/week	Adverse effects include GI upset, stomatitis, alopecia, sloughing of nails, dysuria, bone marrow suppression and pulmonary fibrosis. Dosages >500 mg in cats can cause methemoglobinaemia. Use with caution in Dalmatians or patients with a history of urate stones
Imipramine	Tricyclic antidepressant	Dog: 2–4 mg/kg PO q12–24h Cat: 0.5–1 mg/kg PO q12–24h	See clomipramine

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Drugs used in neurological emergencies *(continued)*

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Ketamine	Dissociative anaesthetic Analgesic	Dog: 10 mcg/kg/minute IV CRI preceded by a 0.25 mg/kg loading dose (intraoperative analgesia); 2–5 mcg/kg/minute IV CRI preceded by a 0.25 mg/kg loading dose (postoperative analgesia); 2 mg/kg IV (induction of anaesthesia in combination with diazepam or midazolam as part of volatile anaesthetic technique); 5–7 mg/kg IV, IM combined with 40 mcg/kg IV, IM medetomidine (induction general anaesthesia) Cat: same dosage as in dog for intra- and postoperative analgesia; 5 mg/kg IM with 0.2 mg/kg IM midazolam or diazepam (chemical restraint)	Contraindicated in patients with hypertension, suspected increased intracranial pressure (e.g. patients with head trauma) or increased intraocular pressure. Also contraindicated in patients with seizure disorders or those undergoing myelography. Can cause hyperthermia in cats. Adverse effects reported with high dosages include respiratory depression, vomiting, muscle tremors, convulsions and cardiac arrest
Lactulose	Laxative	Dog: 10–20 ml/kg of a solution comprising 3 parts lactulose to 7 parts water per rectum as retention enema q6–8h (acute hepatic encephalopathy); 0.5–1 ml/kg PO q8–12h (hepatic encephalopathy) Cat: same dosage as dog for retention enema; 2.5–5 ml/cat PO q8–12h (hepatic encephalopathy)	Adverse effects include flatulence, diarrhoea and abdominal cramping. Overdosage can lead to dehydration. Contains free sugars and may affect insulin requirements in diabetic patients. Do not combine with other laxatives
Levetiracetam	Antiepileptic	Dog: 20–30 mg/kg PO q8h; 20 mg/kg IV q8h (emergency treatment of seizures) Cat: 30 mg/kg PO q12h; 20 mg/kg IV q8h (emergency treatment of seizures)	Reported adverse effects include behaviour changes and sedation. Patients receiving phenobarbital may require higher doses than those not on phenobarbital. Dosages up to 60 mg/kg q8h have been tolerated without adverse effects
Levothyroxine	Thyroid hormone	Dog: 0.02 mg/kg PO q12–24h (adjust dose via monitoring)	Use with caution in patients with hypoadrenocorticism, cardiac disease or diabetes. Increases the action of catecholamines and sympathomimetics and may alter insulin requirements in diabetic patients

(Continued)

Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Lidocaine	Analgesic Antiarrhythmic	Dog: 25–75 mcg/kg/minute IV CRI preceded by loading dose of 1 mg/kg slow IV (intraoperative analgesia); 2–4 mg/kg SC, perineural infiltration (local, regional blockade anaesthesia) Cat: 1–2 mg/kg SC, perineural infiltration (local, regional blockade anaesthesia) Do not exceed 4 mg/kg in dogs and 2 mg/kg in cats whatever the route	Use with caution in patients with heart block, heart failure, liver failure, respiratory depression or hypovolaemia. Rapid administration of an IV bolus can cause hypotension. Adverse effects are dose related and progress from CNS abnormalities (depression, excitability, ataxia, muscle tremors) to ECG abnormalities. Signs of toxicity include nystagmus, seizures, bradycardia and cardiovascular collapse. Do not give the formulation containing epinephrine intravenously
Mannitol	Osmotic diuretic	Dog: 0.5–2.0 g/kg IV CRI over 15–20 minutes (acute cerebral oedema) Cat: same dosage as in dog	Contraindicated in patients with dehydration, anuric renal failure or severe pulmonary oedema. Adverse effects include GI upset and tachycardia. Overdosage causes sodium, potassium and chloride loss. Must be warmed prior to administration and given through a filter to avoid precipitation
Meclizine	Antiemetic	Dog: 12.5–25 mg/dog q24h (motion sickness or vertigo) Cat: 12.5 mg/cat q24h (vertigo)	Can cause sedation or anticholinergic effects. Do not use in patients with glaucoma or urinary obstruction
Medetomidine	Alpha-2 adrenoreceptor agonist Sedative and analgesic	As supplemental analgesia and sedation: Dog: 1–2 mcg/kg/hour Cat: 1–3 mcg/kg/hour For premedication in healthy animals: Dogs: up to 30 mcg/kg Cats: up to 50 mcg/kg Licensed dose for premedication varies with country	Contraindicated in patients with cardiac disease, renal disease or shock. May disinhibit aggressive dogs. Causes bradycardia and pale mucous membranes. Adverse effects include AV block, respiratory depression and hypoglycaemia. Do not combine with anticholinergic drugs. Reversal agent is atipamezole (*Note:* Label dosage is considered high)
Meloxicam	Nonsteroidal anti-inflammatory	Dog: 0.3 mg/kg SC, IM, IV single injection; 0.1 mg/kg PO q24h Cat: 0.2–0.3 mg/kg SC, IM, IV single injection; 0.05 mg/kg PO q24–48h	Most common adverse effect is GI upset. Do not use in dehydrated patients, patients in renal failure or those with bleeding disorders. Do not use concurrently with other NSAIDs or steroids
Methadone	Opioid analgesic Pure OP3 agonist	Dog: 0.2–0.5 mg/kg IM, slow IV q3–6h Cat: 0.2 –0.3 mg/kg IM, slow IV; may need longer dosing interval than dogs	Can cause vomiting, constipation, sedation, bradycardia and respiratory depression. Overdosage can cause profound CNS and/or respiratory depression. Reversal agent is naloxone

(Continued)

Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Methocarbamol	Centrally acting muscle relaxant	Dog: 20–45 mg/kg PO q8h Cat: same dosage as in dog	Adverse effects include sedation, vomiting, salivation, weakness and ataxia. Do not use injectable product in patients with renal disease
Methylprednisolone sodium succinate	Anti-inflammatory Immunosuppressive drug	Dog: 30 mg/kg IV within 8 hours of spinal cord trauma, followed by 5.4 mg/kg/hour IV CRI for 24–48 hours or 15 mg/kg IV at 2 and 6 hours (spinal cord trauma), then q8h for maximum of 48 hours Cat: same dosage as in dog	See dexamethasone
Mexiletine	Class 1b anti-arrhythmic	Dog: 4–8 mg/kg PO q8–12h (myokymia)	Use with caution in patients with AV block, congestive heart failure, hypotension or seizure disorders. Adverse effects include GI upset and CNS abnormalities (trembling, dizziness, depression). Signs of toxicity progress from CNS abnormalities to cardiovascular depression
Midazolam	Sedative Analgesic Benzodiazepine anticonvulsant	Dog: 0.1–0.3 mg/kg IV, IM, PR (emergency management of seizures); 0.1–0.3 mg/kg/hour IV CRI Cat: same dosage as in dog	Use with caution in patients with significant hepatic disease. May cause paradoxical excitation. Overdosage can cause respiratory depression. Reversal agent is flumazenil
Morphine	Opioid analgesic Pure agonist	Dog: 0.2–0.5 mg/kg slow IV, IM, SC q3–6h; CRI: 0.1–0.2 mg/kg/hour preceded by loading dose of 0.2 mg/kg Cat: 0.1–0.2 mg/kg IM, SC; CRI: 0.1 mg/kg/hour preceded by 0.1 mg/kg loading dose. May need longer dosing interval than dogs	Primary adverse effect is respiratory depression. Other adverse effects include vomiting, sedation and hypothermia. Use with caution in patients with renal impairment, hypoadrenocorticism, mast cell disease or elevated intracranial pressure. Overdosage can cause profound CNS and/or respiratory depression. Reversal agent is naloxone. Do not use in patients that have received a selective serotonin reuptake inhibitor or monoamine oxidase inhibitor in the last 14 days
Mycophenolate	Immunosuppressive drug	Dog: 10 mg/kg PO, IV q12h (range: 5–20 mg/kg q12h) Cat: 10 mg/kg q12h (limited reported use)	Not recommended for use concurrently with azathioprine due to similar mechanism of action and increased risk of bone marrow suppression. Must be given slowly IV. Adjust dosage in patients with renal insufficiency. GI upset is the most common adverse effect

(Continued)

Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Neostigmine bromide and neostigmine methylsulphate	Anticholinesterase	Dog: 0.01–0.1 mg/kg IM, IV, SC as needed depending on duration of response (myasthenic crisis); 0.1–0.25 mg/kg PO q4–6h Cat: use not reported in cats, but extrapolation from dogs seems reasonable	Use with caution in patients with cardiac arrhythmias, epilepsy, hyperthyroidism or intestinal or urinary tract obstruction. Adverse effects are dose related and include cholinergic signs (vomiting, salivation, lacrimation, urination, defecation, miosis and agitation); these can progress to cholinergic crisis (hypotension, weakness, bronchospasm, tachycardia or bradycardia). Atropine can be used to reduce adverse effects
Oxymorphone	Opioid analgesic Pure OP3 agonist	Dog: 0.02–0.2 mg/kg IM, SC, IV Cat: 0.02–0.1 mg/kg IM, SC, IV	Primary adverse effects are respiratory depression and bradycardia. Other adverse effects include vomiting, sedation and hypothermia. Use with caution in patients with renal impairment, hypoadrenocorticism or elevated intracranial pressure. Overdosage can cause profound CNS and/or respiratory depression. Reversal agent is naloxone. Do not use in patients that have received a selective serotonin reuptake inhibitor or monoamine oxidase inhibitor in the last 14 days
Pentobarbital	Anaesthetic	Dog: 2–15 mg/kg slow IV bolus to effect, followed by 0.2–1 mg/kg/hour IV CRI (status epilepticus or cluster seizures) Cat: same dosage as in dog	Do not use in patients with significant liver disease. Use with caution in hypovolaemic or anaemic patients. Primary adverse effect is respiratory depression; can also cause hypothermia. Cats appear to be more sensitive to adverse effects. Rapid IV administration can cause respiratory depression. Perivascular injection causes tissue irritation
Phenobarbital	Antiepileptic	Dog: 2–3 mg/kg PO q12h initial dose; 10–20 mg/kg slow IV bolus to effect or divided into 2–4 mg/kg IV bolus q20–30 minutes (status epilepticus, cluster seizures, tremors) Cat: 1–2 mg/kg PO q12h initial dose	Do not use in patients with significant liver disease. Use with caution in hypovolaemic or anaemic patients. Primary adverse effects include respiratory and CNS depression. Rapid IV administration can cause respiratory depression. May cause tissue necrosis if given perivascularly. Idiosyncratic bone marrow hypoplasia has been reported. Adverse effects include ataxia, sedation (usually transient), PU/PD and polyphagia. Hepatotoxicity is rare, but may occur with long-term use in dogs at high serum concentration or as idiosyncratic reaction within 2 weeks of onset of treatment
Phenoxybenzamine	Alpha-adrenergic antagonist	Dog: 0.25–1 mg/kg PO q8–24h Cat: 1.25–5 mg/cat PO q12–24h	Use cautiously in patients with heart disease. Adverse effects include hypotension and GI upset

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Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Phenylpropanolamine	Adrenergic agonist	Dog: 1 mg/kg PO q8–12h Cat: same dosage as in dog	Use with caution in patients with hypertension, heart disease, hyperthyroidism, diabetes mellitus or glaucoma. Adverse effects include restlessness, irritability, hypertension and anorexia; rarely, strokes and cardiotoxicity have been reported
Potassium bromide	Antiepileptic	Dog: maintenance dose 30–40 mg/kg PO q24h; loading dose 600–800 mg/kg PO divided over 5–6 days Cat: use not recommended	Often causes sedation during the first few weeks of treatment. Other adverse effects include PU/PD, polyphagia and GI upset. Pancreatitis has been reported. Signs of toxicity include sedation/stupor, tremors, ataxia, paraparesis, hyporeflexia, anisocoria and muscle pain. Can cause a potentially fatal asthma-like syndrome in cats. Dietary intake of chloride affects serum bromide levels: diets low in chloride can cause bromide toxicity, while diets high in chloride can reduce serum level and may affect seizure control
Prednisolone	Anti-inflammatory Immune modulator	Dog: 0.5–1.0 mg/kg PO, IV, IM q12–24h then taper to 0.5–1 mg/kg PO q48h (anti-inflammatory); 1.1–3.3 mg/kg PO q12h then taper to 0.5–2.2 mg/kg q48h (immunosuppressive); 0.2–0.3 mg/kg PO q24h (replacement therapy) Cat: 1.1 mg/kg PO q12h then taper to 1.1–2.2 mg/kg q48h (anti-inflammatory); 2.2–6.6 mg/kg PO q12h then taper to 2.2–4.4 mg/kg q48h (immunosuppressive)	See dexamethasone
Pregabalin	Antiepileptic Analgesic	Dog: initially 2 mg/kg PO q8–12h gradually increased to 3–4 mg/kg PO q8–12h to effect Cat: no data available in cats	Adverse effects include sedation, ataxia and weakness
Primidone	Antiepileptic	Dog: 5–20 mg/kg PO q12h Cats: do not use	Adverse effects include anxiety and depression at lower serum levels, PU/PD and polyphagia at moderate serum levels and sedation and ataxia at higher serum levels. Long-term use can cause serious hepatic injury. Rarely reported adverse effects include anaemia, dermatitis, hyperventilation, urolith formation and anorexia

(Continued)

Drugs used in neurological emergencies (*continued*)

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Propofol	Anaesthetic	Dog: 2–6 mg/kg slow IV over 60 seconds to effect (anaesthesia induction); 0.1–0.6 mg/kg/minute IV CRI preceded by 3–6 mg/kg slow IV bolus to effect (status epilepticus, tremors) Cat: 3–8 mg/kg for induction of anaesthesia (*Note:* Care with long-term CRI in the cat; not recommended)	Causes transient apnoea, especially if given rapidly. Overdosage can cause severe respiratory and myocardial depression. Repeated daily use in cats can cause Heinz body haemolytic anaemia
Propranolol	Beta-1 adrenoceptor antagonist	Dog: 0.5–1 mg/kg PO q8h (refractory idiopathic tremor syndrome); 0.02–0.06 mg/kg slow IV bolus over 10 minutes (emergency refractory idiopathic tremor syndrome)	Do not use in patients with heart failure, bradyarrhythmias or conduction disturbances, diabetes mellitus, hypoglycaemia or significant renal or liver disease. Adverse effects include bradycardia, hypotension, AV block, hypoglycaemia and bronchoconstriction
Pyridostigmine bromide	Anticholinesterase	Dog: 0.2–3 mg/kg PO q8–12h (titrate to effect) Cat: same dosage as in dog	See neostigmine
Selegiline	Dopamine agonist	Dog: 1 mg/kg PO q24h (narcolepsy); 0.5–1 mg/kg q24h for minimum 2 months (cognitive dysfunction) Cat: 1 mg/kg PO q24h	Adverse effects include vomiting, diarrhoea, anorexia and lethargy; restlessness, salivation, pruritus, tremors and decreased hearing have also been reported. Separate use by 2 weeks from other antidepressants (selective serotonin reuptake inhibitors or tri/tetracyclic antidepressants); do not use concurrently with opioids or amitraz
Sodium bromide (3%)	Antiepileptic	Dog: maintenance dose 30 mg/kg PO q24h; loading dose 900 mg/kg/24 hours CRI Cat: use not recommended	See potassium bromide, although sodium bromide causes fewer GI adverse effects
Tetanus antitoxin	Antitoxin	Dog: 100–1000 U/kg IV, IM, SC near wound site once preceded by 0.1–0.2 ml SC, ID test dose (observe for 30 minutes for signs of anaphylaxis) Cat: same dosage as in dog	IV administration highly associated with anaphylaxis; precede with test dose and have epinephrine, dexamethasone and benadryl on hand
Thiamine (vitamin B1)	Vitamin	Dog: 50–100 mg/dog IM, SC, PO q12–24h Cat: 25 mg/cat IM, SC, PO q12–24h	Can cause soreness at the site of IM injection. Rarely, hypersensitivity has been reported

(Continued)

Drugs used in neurological emergencies *(continued)*

DRUG NAME	DRUG MECHANISM	DOSAGE	ADVERSE EFFECTS AND PRECAUTIONS
Topiramate	Antiepileptic	Dog: 2–10 mg/kg PO q12h Cat: no data available	Adverse effect profile not well known; may cause ataxia, lethargy or abnormal mentation. Avoid concurrent use with carbonic anhydrase inhibitors
Tramadol	Analgesic Opioid agonist Inhibitor of reuptake of serotonin and norepinephrine	Dog: 2–5 mg/kg PO q8–12h Cat: 2–4 mg/kg PO q12h	Adverse effects include sedation and GI upset. Naloxone is not effective in treating overdose. Do not use in patients that have received a selective serotonin reuptake inhibitor or monoamine oxidase inhibitor in the last 14 days
Trazodone	Serotonin-2 antagonist/reuptake inhibitor Antidepressant, anxiolytic	Dog: Initial dose range for first 3 days: <10 kg, <25 mg q8–24h; >10–20 kg, 50 mg q12–24h; >20–40 kg, 100 mg q12–24h; >40 kg, 100 mg q12–24h. Target dose for long-term administration: <10 kg, <50 mg q8–24h; >10–20 kg, 100 mg q8–24h; >20–40 kg, 200 mg q8–24h; >40 kg, 200–300 mg q8–24h. All doses given PO Cats: no information available on use in cats	Do not use concurrently with monoamine oxidase inhibitors. Adverse effects include serotonin toxicity, GI upset, dry mouth and excessive sedation. Do not use in dogs with glaucoma, a history of seizures or urinary retention and severe liver disease. Recommend lower dosage for patients also receiving tramadol
Valproic acid	Antiepileptic	Dog: 60–200 mg/kg PO q8h or 25–100 mg/kg/day PO when administered with phenobarbital	Use with caution in patients with significant liver disease or thrombocytopenia/pathia. Adverse effects reported in humans include sedation, GI upset, hepatotoxicity, bone marrow suppression and pancreatitis
Voriconazole	Triazole antifungal	Dog: loading dose 6 mg/kg IV or PO q12h for 2 days, followed by 3–4 mg/kg PO q12h	Increases risk of toxicity/adverse effects of cyclosporine, phenytoin, phenobarbital and benzodiazepines if given concurrently. Photosensitization, hallucinations and liver damage reported in humans
Zonisamide	Antiepileptic	Dog: 5 mg/kg PO q12h (single AED) and 10 mg/kg PO q12h (add-on AED for dogs already receiving drugs requiring hepatic metabolism) Cat: 5–10 mg/kg PO q12–24h	Adverse effects may include sedation, ataxia and GI upset

APPENDIX 2: UNITS AND REFERENCE RANGES

(*Note:* All reference ranges provided are approximate and may differ slightly from those of the individual laboratory used.)

Common conversion factors

Units provided	Units desired	Conversion factor
lb	kg	0.454
kg	lb	2.2
mmol/l	mg/dl	× MW/10
mg/dl	mmol/l	× 10/MW
mmol/l	mEq/l	× valence
mEq/l	mmol/l	/valence
%	mg/ml	× 10
°C	°F	× 9/5 + 32
°F	°C	–32 × 5/9

Selected biochemical parameters

Parameter	Dog	Cat
Calcium	2.45–2.92 mmol/l (9.8–11.7 mg/dl)	2.27–2.8 mmol/l (9.1–11.2 mg/dl)
Creatine kinase	46–467 U/l	49–688 U/l
Glucose	3.6–6.2 mmol/l (65–112 mg/dl)	3.7–9.3 mmol/l (67–168 mg/dl)
Ionized calcium	1.25–1.50 mmol/l (5.01–6.01 mg/dl)	1.1–1.4 mmol/l (4.41–5.61 mg/dl)
Lactate (lactic acid)	0.5–2.0 mmol/l (4.5–18.0 mg/dl)	0.5–2.0 mmol/l (4.5–18.0 mg/dl)
Potassium	3.9–4.9 mmol/l (3.9–4.9 mEq/l)	3.5–4.8 mmol/l (3.5–4.8 mEq/l)
Protein	54–71 g/l (5.4–7.1 g/dl)	66–86 g/l (6.6–8.6 g/dl)
Sodium	140–150 mmol/l (140–150 mEq/l)	146–157 mmol/l (146–157 mEq/l)

Coagulation test reference ranges

Coagulation parameter	Dog	Cat
Prothrombin time (seconds)	6.8–10.2	9.6–13.2
Partial thromboplastin time (seconds)	10.7–16.4	12.6–15.7
Fibrinogen degradation product (µg/ml)	<5	<5
D-dimers (µg/ml)	<0.2	<0.2
Buccal mucosal bleeding time (minutes)	2–3	2–3

Normal arterial blood gas values

Blood gas parameter	Dog	Cat
pH	7.41 (7.35–7.46)	7.39 (7.31–7.46)
$PaCO_2$ (mmHg)	37 (32–43)	31 (26–36)
PaO_2 (mmHg)	92 (80–105)	107 (95–115)
Bicarbonate (mmol/l)	22 (18–26)	18 (14–22)

APPENDIX 3: BLOOD TRANSFUSION MONITORING SHEET

Label:

Kennel No: _____

Clinician in charge:

Telephone number:

Other phone number:

Reason for transfusion:

Calculation area

Volume of blood to be transfused: _____

$$\text{Volume} = \text{BW (kg)} \times \text{90 (dog) / 70 (cat)} \times \left(\frac{\text{Desired PCV} - \text{Current PCV}}{\text{PCV of donor}} \right)$$

Possible transfusion reactions

(usually occur in first hour)

- Tachycardia
- Bradycardia (cats)
- Pyrexia
- Salivation, vomiting
- Tremors, agitation, vocalization
- Weakness, depression, recumbency
- Dyspnoea
- Pale mucous membranes
- Weak pulse
- Seizures
- Skin changes (swelling/oedema)

If any suspected transfusion reactions are seen, STOP the transfusion and contact clinician immediately

Blood type: _____

Cross-matched donor?: Yes ❑ No ❑

Type of cross-match: _____

Previous transfusions?: Yes ❑ No ❑

Time		Initial transfusion rate ❑ 0.25 ml/kg/hr ❑ Other: _____	Subsequent transfusion rate ❑ 4–10 ml/kg/hr: _____ ❑ Other: _____
Monitoring Heart rate ● Respiratory rate ○ IABP >I< NIBP >I<	200 150 100 50	Monitor patient & TPR every 5–10 mins	Monitor patient & TPR every 30–60 mins
Temp			
PCV			
Notes/observations			

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